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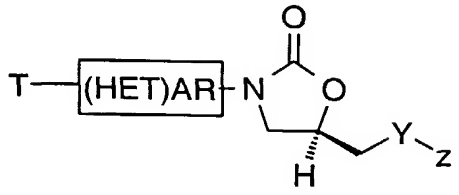
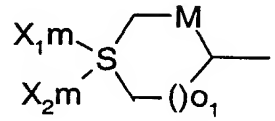
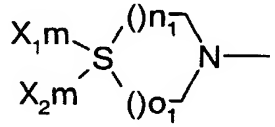
(54) Title: OXAZOLIDINONE-SULFOXIMINES AND -SULFILIMINES AS ANTIBIOTICS



(I)



(TA1)



(TA2)

(57) Abstract: Compounds of formula (I), or a pharmaceutically-acceptable salt, or an in-vivo-hydrolysable ester thereof wherein, for example; T is selected, for example, from a group of the formula (TA1) or (TA2); wherein, for example, X_{1m} is O= and X_{2m} is R_{2s}-$(E)_{ms}$-N-; wherein E is an electron withdrawing group, for example, -SO_2- or -CO-; and, for example, R_{2s} is hydrogen or (1-6C)alkyl; and, for example, HET(AR) is a 5 or 6 membered aromatic or heteroaromatic ring; and, for example, Y is NH and Z is a C5-C6 heteroaromatic ring, for example isoxazolyl, are useful as pharmaceutical agents; and processes for their manufacture and pharmaceutical compositions containing them are described.

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OXAZOLIDINONE-SULFOXIMINES AND -SULFILIMINES AS ANTIBIOTICS

The present invention relates to antibiotic compounds and in particular to antibiotic compounds containing a substituted oxazolidinone ring. This invention further relates to processes for their preparation, to intermediates useful in their preparation, to their use as therapeutic agents and to pharmaceutical compositions containing them.

The international microbiological community continues to express serious concern that the evolution of antibiotic resistance could result in strains against which currently available antibacterial agents will be ineffective. In general, bacterial pathogens may be classified as either Gram-positive or Gram-negative pathogens. Antibiotic compounds with effective activity against both Gram-positive and Gram-negative pathogens are generally regarded as having a broad spectrum of activity. The compounds of the present invention are regarded as effective against both Gram-positive and certain Gram-negative pathogens.

Gram-positive pathogens, for example Staphylococci, Enterococci, and Streptococci are particularly important because of the development of resistant strains which are both difficult to treat and difficult to eradicate from the hospital environment once established. Examples of such strains are methicillin resistant staphylococcus (MRSA), methicillin resistant coagulase negative staphylococci (MRCNS), penicillin resistant Streptococcus pneumoniae and multiply resistant Enterococcus faecium.

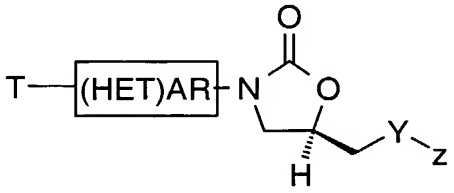
The major clinically effective antibiotic for treatment of such resistant Gram-positive pathogens is vancomycin. Vancomycin is a glycopeptide and is associated with nephrotoxicity and ototoxicity. Furthermore, and most importantly, antibacterial resistance to vancomycin and other glycopeptides is also appearing. This resistance is increasing at a steady rate rendering these agents less and less effective in the treatment of Gram-positive pathogens. There is also now increasing resistance appearing towards agents such as β-lactams, quinolones and macrolides used for the treatment of upper respiratory tract infections, also caused by certain Gram negative strains including H.influenzae and M.catarrhalis.

Certain antibacterial compounds containing an oxazolidinone ring have been described in the art (for example, Walter A. Gregory et al in J.Med.Chem. 1990, 33, 2569-2578 and Chung-Ho Park et al in J.Med.Chem. 1992, 35, 1156-1165).

Such antibacterial oxazolidinone compounds with a 5-acetamidomethyl sidechain may be subject to mammalian peptidase metabolism. Furthermore, bacterial resistance to known antibacterial agents may develop, for example, by (i) the evolution of active binding sites in the bacteria rendering a previously active pharmacophore less effective or redundant, and/or (ii) the evolution of means to chemically deactivate a given pharmacophore. Therefore, there remains an ongoing need to find new antibacterial agents with a favourable pharmacological profile, in particular for compounds containing new pharmacophores.

We have discovered a new class of antibiotic compounds containing an aryl substituted oxazolidinone ring in which the aryl ring is itself substituted by certain novel sulfilimine and sulfoximine-containing rings. These compounds have useful activity against Gram-positive pathogens including MRSA and MRCNS and, in particular, against various strains exhibiting resistance to vancomycin and against E. faecium strains resistant to both aminoglycosides and clinically used β-lactams, but also to fastidious Gram negative strains such as H.influenzae, M.catarrhalis, mycoplasma spp. and chlamydial strains.

Accordingly the present invention provides a compound of the formula (I), or a pharmaceutically-acceptable salt, or an in-vivo-hydrolysable ester thereof,

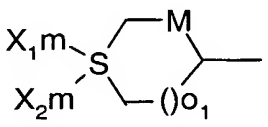


(I)

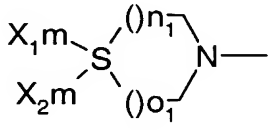
wherein:

T is selected from the groups in (TA) & (TB) below (wherein AR1, AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a, and CY are defined hereinbelow);

(TA) T is selected from the following groups (TA1) and (TA2) :-



(TA1)



(TA2)

wherein :

in (TA1), $()o_1$ is 0 or 1 and represents a chain of carbon atoms (optionally substituted as defined for AR1) of length o_1 and M is a bond joining the adjacent carbon atoms, or M represents one or two carbon atoms, and defines a 4- to 7-membered monocyclic ring, which ring may optionally have one of

(i) one double bond between any two ring carbon atoms; or

(ii) a C1-C3 bridge connecting any two appropriate, non-adjacent ring carbon atoms, which bridge may optionally contain one heteroatom selected from oxygen or >NRc; or

(iii) a C2-C5 cyclic moiety including a ring carbon atom to define a spiro C2-C5 ring system, which ring may optionally contain one heteroatom selected from oxygen or >NRc; or

(iv) a C1-C4 bridge connecting adjacent carbon atoms to define a fused ring, wherein a C2-C4 bridge may optionally contain one heteroatom selected from oxygen or >NRc; wherein Rc is as defined hereinafter;

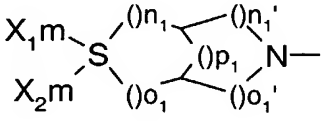
wherein in (TA2), $()n_1$ and $()o_1$ are independently 0, 1 or 2 and represent chains of carbon atoms (optionally substituted as defined for AR1) of length n_1 and o_1 respectively, and define a 4- to 8-membered monocyclic ring, which ring may optionally have one of

(i) a C1-C3 bridge connecting any two appropriate, non-adjacent ring carbon atoms, which bridge contains one heteroatom selected from oxygen or >NRc; or

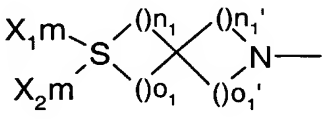
(ii) a C2-C5 cyclic moiety including a ring carbon atom to define a spiro C2-C5 ring system, which ring may optionally contain one heteroatom selected from oxygen or >NRc; or

(iii) a C1-C4 bridge connecting adjacent carbon atoms to define a fused ring, wherein a C2-C4 bridge may optionally contain one heteroatom selected from oxygen or >NRc; wherein Rc is as defined hereinafter; or

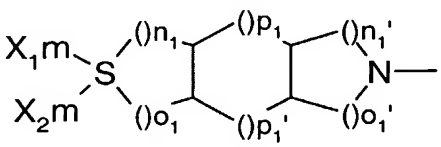
(TB) T is selected from the following groups (TB1) to (TB3) :-



(TB1)



(TB2)



(TB3)

wherein $()n_1$, $()o_1$, $()n_{1'}$, $()o_{1'}$, $()p_1$ and $()p_{1'}$ represent chains of carbon atoms (optionally substituted as defined for AR1 hereinafter) of length n_1, o_1, $n_{1'}$, $o_{1'}$, p_1 and $p_{1'}$ respectively, and are independently 0-2, with the proviso that in (TB1) and (TB2) the sum of n_1, o_1, $n_{1'}$ and $o_{1'}$ does not exceed 8 (giving a maximum ring size of 14 in (TB1) and 11 in (TB2)), and in (TB3) the sum of n_1, o_1, $n_{1'}$, $o_{1'}$, p_1 and $p_{1'}$ does not exceed 6 (giving a maximum ring size of 12);

X_{1m} and X_{2m} taken together represent R_{2s}-$(E)_{ms}$-N=; or

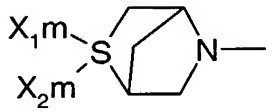
X_{1m} is O= and X_{2m} is R_{2s}-$(E)_{ms}$-N-, and vice versa;

wherein E is an electron withdrawing group selected from -SO_2-, -CO-, -O-CO-, -CO-O-, -CS-, -$CON(R_s)$-, -$SO_2N(R_s)$-, or E may represent a group of the formula R_{3s}-C(=N-O-R_{3s})-C(=O)-, wherein R_{3s} is H or as defined in R_{2s} at (i) below;

or, when E is -$CON(R_s)$- or -$SO_2N(R_s)$-, R_{2s} and R_s may link together to form a carbon chain which defines a 5- or 6-membered saturated, unsaturated or partially unsaturated ring linked via the N atom in E, which ring is optionally further substituted by an oxo substituent, and which ring may be optionally fused with a phenyl group to form a benzo-fused system, wherein the phenyl group is optionally substituted by up to three substituents independently selected from halo, cyano, (1-4C)alkyl and (1-4C)alkoxy;

ms is 0 or 1;

except that, wherein in (TA1) (other than as defined in (i) – (iv) above), in (TA2) (other than as defined in (i) - (iii) above), or in (TB1) when TB1 is TB1b:



TB1b

and X_{1m} is O= and X_{2m} is R_{2s}-$(E)_{ms}$-N-, or vice versa,

R_{2s}-$(E)_{ms}$- may not be hydrogen, (1-4C)alkyl (optionally substituted as defined for R_p below), -C(=O)(1-4C)alkyl (optionally substituted as defined for R_p below), -C(=O)O(1-4C)alkyl (optionally substituted as defined for R_p below), -$C(=O)NHR_p$, or –$C(=S)NHR_p$,

wherein R_p is hydrogen, (1-4C)alkyl (optionally substituted with one or more halo, cyano, nitro, phenyl, (3-6C)cycloalkyl, OR_{p2}, $C(=O)R_{p2}$, $OC(=O)R_{p2}$, $C(=O)OR_{p2}$, $S(=O)_{mp}R_{p2}$, $S(=O)_{mp}NR_{p2}R_{p2}$, $NR_{p2}SO_2R_{p2}$, $NR_{p2}NSO_2R_{p2}R_{p2}$, $NR_{p2}C(=O)R_{p2}$, $C(=O)NR_{p2}R_{p2}$, $NR_{p2}R_{p2}$,

oxo or oxime) or phenyl,

wherein R_{p2} is hydrogen, (1-4C)alkyl or phenyl,

wherein at each occurrence phenyl is optionally substituted with one or more halo, cyano, nitro, phenyl, (3-6C)cycloalkyl, OR_{p2}, $C(=O)R_{p2}$, $OC(=O)R_{p2}$, $C(=O)OR_{p2}$, $S(=O)_{mp}R_{p2}$, $S(=O)_{mp}NR_{p2}R_{p2}$, $NR_{p2}SO_2R_{p2}$, $NR_{p2}NSO_2R_{p2}R_{p2}$, $NR_{p2}C(=O)R_{p2}$, $C(=O)NR_{p2}R_{p2}$, or $NR_{p2}R_{p2}$,

and mp is 0, 1 or 2;

R_{2s} and R_s are independently selected from :

(i) hydrogen (except where E is $-SO_2-$ or -O-CO-), or

(1-6C)alkyl {optionally substituted by one or more (1-4C)alkanoyl groups (including geminal disubstitution) and/or optionally monosubstituted by cyano, cyano-imino, (1-4C)alkoxy, trifluoromethyl, (1-4C)alkoxycarbonyl, phenyl (optionally substituted as defined for AR1 hereinafter), optionally substituted heteroaryl group of the formula AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a or CY all as defined (and optionally substituted as defined) hereinafter, (1-4C)alkyl$S(O)_q$- (q is 0, 1 or 2); and/or (with the proviso that where R_{2s} is $-SO_2$ or -O-CO- not on the first carbon atom of the (1-6C) alkyl chain) optionally substituted by one or more groups (including geminal disubstitution) each independently selected from hydroxy and fluoro, and/or optionally further substituted, by no more than one of each of, oxo, -NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl], (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino, N-(1-4C)alkyl-N-(1-6C)alkanoylamino, (1-4C)alkyl$S(O)_p$NH- or (1-4C)alkyl$S(O)_p$-((1-4C)alkyl)N- (p is 1 or 2)}; or

(ii) an optionally substituted aryl or optionally substituted heteroaryl group of the formula AR1, AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a or CY all as defined (and optionally substituted as defined) hereinafter;

or (where ms is 0 only);

(iii) cyano, -CO-NRvRw, -CO-NRv Rw', $-SO_2$-NRvRw, $-SO_2$-NRv Rw' [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl; Rw' is phenyl (optionally substituted as defined for AR1 hereinafter), or a heteroaryl group selected from AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a (optionally substituted as defined hereinafter)], (1-4C)alkoxycarbonyl, trifluoromethyl, ethenyl, 2-(1-4C)alkylethenyl, 2-cyanoethenyl, 2-cyano-2-((1-4C)alkyl)ethenyl, 2-nitroethenyl, 2-nitro-2-((1-4C)alkyl)ethenyl, 2-((1-

4C)alkylaminocarbonyl)ethenyl, 2-((1-4C)alkoxycarbonyl)ethenyl, 2-(AR1)ethenyl, 2-(AR2)ethenyl, or 2-(AR2a)ethenyl;

wherein Rc is selected from groups (Rc1) to (Rc5) :-

(Rc1) (1-6C)alkyl {optionally substituted by one or more (1-4C)alkanoyl groups (including geminal disubstitution) and/or optionally monosubstituted by cyano, (1-4C)alkoxy, trifluoromethyl, (1-4C)alkoxycarbonyl, phenyl (optionally substituted as for AR1 defined hereinafter), (1-4C)alkyl$S(O)_q$- (q is 0, 1 or 2); or, on any but the first carbon atom of the (1-6C)alkyl chain, optionally substituted by one or more groups (including geminal disubstitution) each independently selected from hydroxy and fluoro, and/or optionally monosubstituted by oxo, -NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl], (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino, N-(1-4C)alkyl-N-(1-6C)alkanoylamino, (1-4C)alkyl$S(O)_p$NH- or (1-4C)alkyl$S(O)_p$-((1-4C)alkyl)N- (p is 1 or 2)};

(Rc2) $R^{13}CO$- , $R^{13}SO_2$- or $R^{13}CS$-

wherein R^{13} is selected from (Rc2a) to (Rc2e) :-

(Rc2a) AR1, AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a, CY;

(Rc2b) hydrogen, (1-4C)alkoxycarbonyl, trifluoromethyl, -NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl], ethenyl, 2-(1-4C)alkylethenyl, 2-cyanoethenyl, 2-cyano-2-((1-4C)alkyl)ethenyl, 2-nitroethenyl, 2-nitro-2-((1-4C)alkyl)ethenyl, 2-((1-4C)alkylaminocarbonyl)ethenyl, 2-((1-4C)alkoxycarbonyl)ethenyl, 2-(AR1)ethenyl, 2-(AR2)ethenyl, 2-(AR2a)ethenyl;

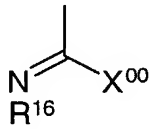
(Rc2c) (1-10C)alkyl {optionally substituted by one or more groups (including geminal disubstitution) each independently selected from hydroxy, (1-10C)alkoxy, (1-4C)alkoxy-(1-4C)alkoxy, (1-4C)alkoxy-(1-4C)alkoxy-(1-4C)alkoxy, (1-4C)alkanoyl, carboxy, phosphoryl [-O-P(O)$(OH)_2$, and mono- and di-(1-4C)alkoxy derivatives thereof], phosphiryl [-O-P$(OH)_2$ and mono- and di-(1-4C)alkoxy derivatives thereof], and amino; and/or optionally substituted by one group selected from phosphonate [phosphono, -P(O)$(OH)_2$, and mono- and di-(1-4C)alkoxy derivatives thereof], phosphinate [-P$(OH)_2$ and mono- and di-(1-4C)alkoxy derivatives thereof], cyano, halo, trifluoromethyl, (1-4C)alkoxycarbonyl, (1-4C)alkoxy-(1-4C)alkoxycarbonyl, (1-4C)alkoxy-(1-4C)alkoxy-(1-4C)alkoxycarbonyl, (1-4C)alkylamino, di((1-4C)alkyl)amino, (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino, N-(1-4C)alkyl-N-(1-6C)alkanoylamino, (1-4C)alkylaminocarbonyl, di((1-4C)alkyl)aminocarbonyl, (1-

4C)alkylS(O)$_p$NH-, (1-4C)alkylS(O)$_p$-((1-4C)alkyl)N-, fluoro(1-4C)alkylS(O)$_p$NH-, fluoro(1-4C)alkylS(O)$_p$((1-4C)alkyl)N-, (1-4C)alkylS(O)$_q$- [the (1-4C)alkyl group of (1-4C)alkylS(O)$_q$- being optionally substituted by one substituent selected from hydroxy, (1-4C)alkoxy, (1-4C)alkanoyl, phosphoryl [-O-P(O)(OH)$_2$, and mono- and di-(1-4C)alkoxy derivatives thereof], phosphiryl [-O-P(OH)$_2$ and mono- and di-(1-4C)alkoxy derivatives thereof], amino, cyano, halo, trifluoromethyl, (1-4C)alkoxycarbonyl, (1-4C)alkoxy-(1-4C)alkoxycarbonyl, (1-4C)alkoxy-(1-4C)alkoxy-(1-4C)alkoxycarbonyl, carboxy, (1-4C)alkylamino, di((1-4C)alkyl)amino, (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino, N-(1-4C)alkyl-N-(1-6C)alkanoylamino, (1-4C)alkylaminocarbonyl, di((1-4C)alkyl)aminocarbonyl, (1-4C)alkylS(O)$_p$NH-, (1-4C)alkylS(O)$_p$-((1-4C)alkyl)N-, (1-4C)alkylS(O)$_q$-, AR1-S(O)$_q$- , AR2-S(O)$_q$- , AR3-S(O)$_q$- and also AR2a, AR2b, AR3a and AR3b versions of AR2 and AR3 containing groups], CY, AR1, AR2, AR3, AR1-O-, AR2-O-, AR3-O-, AR1-S(O)$_q$- , AR2-S(O)$_q$- , AR3-S(O)$_q$- , AR1-NH-, AR2-NH-, AR3-NH- (p is 1 or 2 and q is 0, 1 or 2), and also AR2a, AR2b, AR3a and AR3b versions of AR2 and AR3 containing groups};

(Rc2d) R^{14}C(O)O(1-6C)alkyl wherein R^{14} is AR1, AR2, (1-4C)alkylamino (the (1-4C)alkyl group being optionally substituted by (1-4C)alkoxycarbonyl or by carboxy), benzyloxy-(1-4C)alkyl or (1-10C)alkyl {optionally substituted as defined for (Rc2c)};

(Rc2e) R^{15}O- wherein R^{15} is benzyl, (1-6C)alkyl {optionally substituted as defined for (Rc2c)}, CY, or AR2b;

(Rc3) hydrogen, cyano, 2-cyanoethenyl, 2-cyano-2-((1-4C)alkyl)ethenyl, 2-((1-4C)alkylaminocarbonyl)ethenyl, 2-((1-4C)alkoxycarbonyl)ethenyl, 2-nitroethenyl, 2-nitro-2-((1-4C)alkyl)ethenyl, 2-(AR1)ethenyl, 2-(AR2)ethenyl, or of the formula **(Rc3a)**



(Rc3a)

wherein X^{00} is -OR^{17}, -SR^{17}, -$NHR^{17}$and -$N(R^{17})_2$;

wherein R^{17} is hydrogen (when X^{00} is -$NHR^{17}$and -$N(R^{17})_2$), and R^{17} is (1-4C)alkyl, phenyl or AR2 (when X^{00} is -OR^{17}, -SR^{17} and -NHR^{17}); and R^{16} is cyano, nitro, (1-4C)alkylsulfonyl, (4-7C)cycloalkylsulfonyl, phenylsulfonyl, (1-4C)alkanoyl and (1-4C)alkoxycarbonyl;

(Rc4) trityl, AR1, AR2, AR2a, AR2b, AR3, AR3a, AR3b;

(Rc5) RdOC(Re)=CH(C=O)-, RfC(=O)C(=O)-, RgN=C(Rh)C(=O)- or RiNHC(Rj)=CHC(=O)- wherein Rd is (1-6C)alkyl; Re is hydrogen or (1-6C)alkyl, or Rd and Re together form a (3-4C)alkylene chain; Rf is hydrogen, (1-6C)alkyl, hydroxy(1-6C)alkyl, (1-6C)alkoxy(1-6C)alkyl, -NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl], (1-6C)alkoxy, (1-6C)alkoxy(1-6C)alkoxy, hydroxy(2-6C)alkoxy, (1-4C)alkylamino(2-6C)alkoxy, di-(1-4C)alkylamino(2-6C)alkoxy; Rg is (1-6C)alkyl, hydroxy or (1-6C)alkoxy; Rh is hydrogen or (1-6C)alkyl; Ri is hydrogen, (1-6C)alkyl, AR1, AR2, AR2a, AR2b and Rj is hydrogen or (1-6C)alkyl;

wherein

AR1 is an optionally substituted phenyl or optionally substituted naphthyl;

AR2 is an optionally substituted 5- or 6-membered, fully unsaturated (i.e with the maximum degree of unsaturation) monocyclic heteroaryl ring containing up to four heteroatoms independently selected from O, N and S (but not containing any O-O, O-S or S-S bonds), and linked via a ring carbon atom, or a ring nitrogen atom if the ring is not thereby quaternised;

AR2a is a partially hydrogenated version of AR2 (i.e. AR2 systems retaining some, but not the full, degree of unsaturation), linked via a ring carbon atom or linked via a ring nitrogen atom if the ring is not thereby quaternised;

AR2b is a fully hydrogenated version of AR2 (i.e. AR2 systems having no unsaturation), linked via a ring carbon atom or linked via a ring nitrogen atom;

AR3 is an optionally substituted 8-, 9- or 10-membered, fully unsaturated (i.e with the maximum degree of unsaturation) bicyclic heteroaryl ring containing up to four heteroatoms independently selected from O, N and S (but not containing any O-O, O-S or S-S bonds), and linked via a ring carbon atom in either of the rings comprising the bicyclic system;

AR3a is a partially hydrogenated version of AR3 (i.e. AR3 systems retaining some, but not the full, degree of unsaturation), linked via a ring carbon atom, or linked via a ring nitrogen atom if the ring is not thereby quaternised, in either of the rings comprising the bicyclic system;

AR3b is a fully hydrogenated version of AR3 (i.e. AR3 systems having no unsaturation), linked via a ring carbon atom, or linked via a ring nitrogen atom, in either of the rings comprising the bicyclic system;

AR4 is an optionally substituted 13- or 14-membered, fully unsaturated (i.e with the

maximum degree of unsaturation) tricyclic heteroaryl ring containing up to four heteroatoms independently selected from O, N and S (but not containing any O-O, O-S or S-S bonds), and linked via a ring carbon atom in any of the rings comprising the tricyclic system;

AR4a is a partially hydrogenated version of AR4 (i.e. AR4 systems retaining some, but not the full, degree of unsaturation), linked via a ring carbon atom, or linked via a ring nitrogen atom if the ring is not thereby quaternised, in any of the rings comprising the tricyclic system;

CY is an optionally substituted cyclobutyl, cyclopentyl, cyclohexyl, cyclopentenyl or cyclohexenyl ring;

For the avoidance of doubt in the definition of (TA1) & (TA2) and (TB), it is to be understood that when R_{2s} and R_s are independently selected from

(ii) (1-6C)alkyl {optionally substituted, for example, by no more than one of each of oxo and -NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl], to avoid duplication with the substituent -CO-NRvRw provided in section (iii) of the definition for R_{2s} and R_s, then oxo and -NRvRw are not to be both selected together when (1-6C)alkyl is methyl;

(HET)AR is a 5-6 membered aromatic or heteroaromatic ring, (i) when a 5-membered ring this may be a thiophene ring, comprising a single sulphur atom sited ortho to the nitrogen atom on the adjacent oxazolidinone ring, such a ring may have a single optional substituent R1 as hereinafter defined sited ortho to the carbon atom on the adjacent sulfilimine/sulfoximine ring, (ii) when a 6-membered ring this may be a phenyl ring or comprise a single nitrogen atom sited ortho to the nitrogen atom on the adjacent oxazolidinone ring, such ring may be optionally substituted at one or both positions ortho to the carbon atom on the adjacent sulfilimine/sulfoximine ring by R1, where each

R1 is independently selected from hydrogen, halogen, methyl and methoxy, ethyl and ethoxy;

Y is -NR4- wherein R4 is hydrogen, or (1-6C)alkyl or -COOR5 wherein R5 is (1-6C) alkyl optionally substituted by one or more chlorine atoms;

Z is a C5-C6 heteroaromatic ring joined to Y via a ring carbon atom, which ring is optionally substituted on an available carbon atom by 1 or 2 substituents independently selected from (1-4C)alkyl, amino, (1-4C)alkylamino, (1-4C)alkoxy and halogen, and/or on an available nitrogen atom (provided that the ring is not thereby quaternised) by (1-4C)alkyl.

For the avoidance of doubt, in the above definitions of TA1, TA2 and TB, $()n_1$, $()o_1$, $()n_1'$, $()o_1'$, $()p_1$ and $()p_1$ indicate (-CH2-)n_1, (-CH2-)o_1, (-CH2-)n_1', (-CH2)o_1', (-CH2-)p_1 and (-CH2-)p_1' respectively.

In this specification the term 'alkyl' includes straight chained and branched structures. For example, (1-6C)alkyl includes propyl, isopropyl and tert-butyl. However, references to individual alkyl groups such as "propyl" are specific for the straight chained version only, and references to individual branched chain alkyl groups such as "isopropyl" are specific for the branched chain version only. A similar convention applies to other radicals, for example halo(1-4C)alkyl includes 1-bromoethyl and 2-bromoethyl.

The term "a C5-C6 heteroaromatic ring" means a 5- or 6-membered aryl ring wherein (unless stated otherwise) 1, 2 or 3 of the ring atoms are selected from nitrogen, oxygen and sulfur. Unless stated otherwise, such rings are fully aromatic. Particular examples of 5- or 6-membered heteroaryl ring systems are furan, pyrrole, pyrazole, imidazole, triazole, pyrimidine, pyridazine, pyridine, isoxazole, oxazole, isothiazole, thiazole and thiophene.

In general "halogen" when present as an aromatic ring substituent is selected from any one of bromine, chlorine or fluorine, as an aliphatic substituent from chlorine or fluorine.

Particular optional substituents for alkyl, phenyl (and phenyl containing moieties) and naphthyl groups and ring carbon atoms in heteroaryl (mono or bicyclic) rings (such as set out hereinafter in groups AR1 to CY inclusive) include halo, (1-4C)alkyl , hydroxy, nitro, carbamoyl, (1-4C)alkylcarbamoyl, di-((1-4C)alkyl)carbamoyl, cyano, trifluoromethyl, trifluoromethoxy, amino, (1-4C)alkylamino, di((1-4C)alkyl)amino, (1-4C)alkyl $S(O)_q$- (q is 0, 1 or 2), carboxy, (1-4C)alkoxycarbonyl, (2-4C)alkenyl, (2-4C)alkynyl, (1-4C)alkanoyl, (1-4C)alkoxy, (1-4C)alkyl$S(O)_2$amino, (1-4C)alkanoylamino, benzoylamino, benzoyl, phenyl (optionally substituted by up to three substituents selected from halo, (1-4C)alkoxy or cyano), furan, pyrrole, pyrazole, imidazole, triazole, pyrimidine, pyridazine, pyridine, isoxazole, oxazole, isothiazole, thiazole, thiophene, hydroxyimino(1-4C)alkyl, (1-4C)alkoxyimino(1-4C)alkyl, hydroxy-(1-4C)alkyl, halo-(1-4C)alkyl, nitro(1-4C)alkyl, amino(1-4C)alkyl, cyano(1-4C)alkyl, (1-4C)alkanesulfonamido, aminosulfonyl, (1-4C)alkylaminosulfonyl and di-((1-4C)alkyl)aminosulfonyl. The phenyl and naphthyl groups and heteroaryl (mono- or bicyclic) rings may be mono- or di-substituted on ring carbon atoms with substituents

independently selected from the above list of particular optional substituents, or on ring nitrogen atoms provided the ring is not thereby quaternised.

Particular examples of 5-membered heteroaryl rings containing 2 or 3 heteroatoms independently selected from N, O and S (with the proviso that there are no O-O, O-S or S-S bonds) are pyrazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, oxazole, isoxazole, thiazole, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole; and also in an alternative embodiment, isothiazole, 1,2,5-thiadiazole, 1,2,4-thiadiazole or 1,2,3-thiadiazole.

There follow particular and suitable values for certain substituents and groups referred to in this specification. These values may be used where appropriate with any of the definitions and embodiments disclosed hereinbefore, or hereinafter. For the avoidance of doubt each stated species represents a particular and independent aspect of this invention.

Examples of **(1-4C)alkyl** and **(1-5C)alkyl** include methyl, ethyl, and propyl and isopropyl; examples of **(1-6C)alkyl** include methyl, ethyl, propyl, isopropyl, pentyl and hexyl; examples of **(1-10C)alkyl** include methyl, ethyl, propyl, isopropyl, pentyl, hexyl, heptyl, octyl and nonyl; examples of **(1-4C)alkanoylamino-(1-4C)alkyl** include formamidomethyl, acetamidomethyl and acetamidoethyl; examples of **hydroxy(1-4C)alkyl** and **hydroxy(1-6C)alkyl** include hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl and 3-hydroxypropyl; examples of **(1-4C)alkoxycarbonyl** include methoxycarbonyl, ethoxycarbonyl and propoxycarbonyl; examples of **2-((1-4C)alkoxycarbonyl)ethenyl** include 2-(methoxycarbonyl)ethenyl and 2-(ethoxycarbonyl)ethenyl; examples of **2-cyano-2-((1-4C)alkyl)ethenyl** include 2-cyano-2-methylethenyl and 2-cyano-2-ethylethenyl; examples of **2-nitro-2-((1-4C)alkyl)ethenyl** include 2-nitro-2-methylethenyl and 2-nitro-2-ethylethenyl; examples of **2-((1-4C)alkylaminocarbonyl)ethenyl** include 2-(methylaminocarbonyl)ethenyl and 2-(ethylaminocarbonyl)ethenyl; examples of **(2-4C)alkenyl** include allyl and vinyl; examples of **(2-4C)alkynyl** include ethynyl and 2-propynyl; examples of **(1-4C)alkanoyl** include formyl, acetyl and propionyl; examples of **(1-4C)alkoxy** include methoxy, ethoxy and propoxy; examples of **(1-6C)alkoxy** and **(1-10C)alkoxy** include methoxy, ethoxy, propoxy and pentoxy; examples of **(1-4C)alkylthio** include methylthio and ethylthio; examples of **(1-4C)alkylamino** include methylamino, ethylamino and propylamino; examples of **di-((1-4C)alkyl)amino** include dimethylamino, N-ethyl-N-methylamino, diethylamino, N-methyl-N-propylamino and dipropylamino; examples of **halo** groups include fluoro, chloro and bromo; examples of **(1-4C)alkylsulfonyl** include methylsulfonyl and ethylsulfonyl; examples of **(1-**

4C)alkoxy-(1-4C)alkoxy and **(1-6C)alkoxy-(1-6C)alkoxy** include methoxymethoxy, 2-methoxyethoxy, 2-ethoxyethoxy and 3-methoxypropoxy; examples of **(1-4C)alkoxy-(1-4C)alkoxy-(1-4C)alkoxy** include 2-(methoxymethoxy)ethoxy, 2-(2-methoxyethoxy)ethoxy; 3-(2-methoxyethoxy)propoxy and 2-(2-ethoxyethoxy)ethoxy; examples of **(1-4C)alkylS(O)$_2$amino** include methylsulfonylamino and ethylsulfonylamino; examples of **(1-4C)alkanoylamino** and **(1-6C)alkanoylamino** include formamido, acetamido and propionylamino; examples of **(1-4C)alkoxycarbonylamino** include methoxycarbonylamino and ethoxycarbonylamino; examples of **N-(1-4C)alkyl-N-(1-6C)alkanoylamino** include N-methylacetamido, N-ethylacetamido and N-methylpropionamido; examples of **(1-4C)alkylS(O)$_p$NH-** wherein p is 1 or 2 include methylsulfinylamino, methylsulfonylamino, ethylsulfinylamino and ethylsulfonylamino; examples of **(1-4C)alkylS(O)$_p$((1-4C)alkyl)N-** wherein p is 1 or 2 include methylsulfinylmethylamino, methylsulfonylmethylamino, 2-(ethylsulfinyl)ethylamino and 2-(ethylsulfonyl)ethylamino; examples of **fluoro(1-4C)alkylS(O)$_p$NH-** wherein p is 1 or 2 include trifluoromethylsulfinylamino and trifluoromethylsulfonylamino; examples of **fluoro(1-4C)alkylS(O)$_p$((1-4C)alkyl)NH-** wherein p is 1 or 2 include trifluoromethylsulfinylmethylamino and trifluoromethylsulfonylmethylamino examples of **(1-4C)alkoxy(hydroxy)phosphoryl** include methoxy(hydroxy)phosphoryl and ethoxy(hydroxy)phosphoryl; examples of **di-(1-4C)alkoxyphosphoryl** include di-methoxyphosphoryl, di-ethoxyphosphoryl and ethoxy(methoxy)phosphoryl;

examples of **(1-4C)alkylS(O)$_q$-** wherein q is 0, 1 or 2 include methylthio, ethylthio, methylsulfinyl, ethylsulfinyl, methylsulfonyl and ethylsulfonyl; examples of **phenylS(O)$_q$** and **naphthylS(O)$_q$-** wherein q is 0, 1 or 2 are phenylthio, phenylsulfinyl, phenylsulfonyl and naphthylthio, naphthylsulfinyl and naphthylsulfonyl respectively; examples of **benzyloxy-(1-4C)alkyl** include benzyloxymethyl and benzyloxyethyl; examples of a **(3-4C)alkylene** chain are trimethylene or tetramethylene; examples of **(1-6C)alkoxy-(1-6C)alkyl** include methoxymethyl, ethoxymethyl and 2-methoxyethyl; examples of **hydroxy-(2-6C)alkoxy** include 2-hydroxyethoxy and 3-hydroxypropoxy; examples of **(1-4C)alkylamino-(2-6C)alkoxy** include 2-methylaminoethoxy and 2-ethylaminoethoxy; examples of **di-(1-4C)alkylamino-(2-6C)alkoxy** include 2-dimethylaminoethoxy and 2-diethylaminoethoxy; examples of **phenyl(1-4C)alkyl** include benzyl and phenethyl; examples of **(1-**

4C)alkylcarbamoyl include methylcarbamoyl and ethylcarbamoyl; examples of **di((1-4C)alkyl)carbamoyl** include di(methyl)carbamoyl and di(ethyl)carbamoyl; examples of **hydroxyimino(1-4C)alkyl** include hydroxyiminomethyl, 2-(hydroxyimino)ethyl and 1-(hydroxyimino)ethyl; examples of **(1-4C)alkoxyimino-(1-4C)alkyl** include methoxyiminomethyl, ethoxyiminomethyl, 1-(methoxyimino)ethyl and 2-(methoxyimino)ethyl; examples of **halo(1-4C)alkyl** include, halomethyl, 1-haloethyl, 2-haloethyl, and 3-halopropyl; examples of **nitro(1-4C)alkyl** include nitromethyl, 1-nitroethyl, 2-nitroethyl and 3-nitropropyl; examples of **amino(1-4C)alkyl** include aminomethyl, 1-aminoethyl, 2-aminoethyl and 3-aminopropyl; examples of **cyano(1-4C)alkyl** include cyanomethyl, 1-cyanoethyl, 2-cyanoethyl and 3-cyanopropyl; examples of **(1-4C)alkanesulfonamido** include methanesulfonamido and ethanesulfonamido; examples of **(1-4C)alkylaminosulfonyl** include methylaminosulfonyl and ethylaminosulfonyl; and examples of **di-(1-4C)alkylaminosulfonyl** include dimethylaminosulfonyl, diethylaminosulfonyl and N-methyl-N-ethylaminosulfonyl; examples of **(1-4C)alkanesulfonyloxy** include methylsulfonyloxy, ethylsulfonyloxy and propylsulfonyloxy; examples of **(1-4C)alkanoyloxy** include acetoxy; examples of **(1-4C)alkylaminocarbonyl** include methylaminocarbonyl and ethylaminocarbonyl; examples of **di((1-4C)alkyl)aminocarbonyl** include dimethylaminocarbonyl and diethylaminocarbonyl; examples of **(3-6C)cycloalkyl and (3-8C)cycloalkyl** include cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl; examples of **(4-7C)cycloalkyl** include cyclobutyl, cyclopentyl and cyclohexyl; examples of **di(N-(1-4C)alkyl)aminomethylimino** include dimethylaminomethylimino and diethylaminomethylimino.

Particular values for AR2 include, for example, for those AR2 containing one heteroatom, furan, pyrrole, thiophene; for those AR2 containing one to four N atoms, pyrazole, imidazole, pyridine, pyrimidine, pyrazine, pyridazine, 1,2,3- & 1,2,4-triazole and tetrazole; for those AR2 containing one N and one O atom, oxazole, isoxazole and oxazine; for those AR2 containing one N and one S atom, thiazole and isothiazole; for those AR2 containing two N atoms and one S atom, 1,2,4- and 1,3,4-thiadiazole.

Particular examples of AR2a include, for example, dihydropyrrole (especially 2,5-dihydropyrrol-4-yl) and tetrahydropyridine (especially 1,2,5,6-tetrahydropyrid-4-yl).

Particular examples of AR2b include, for example, tetrahydrofuran, pyrrolidine, morpholine (preferably morpholino), thiomorpholine (preferably thiomorpholino), piperazine

(preferably piperazino), imidazoline and piperidine, 1,3-dioxolan-4-yl, 1,3-dioxan-4-yl, 1,3-dioxan-5-yl and 1,4-dioxan-2-yl.

Particular values for AR3 include, for example, bicyclic benzo-fused systems containing a 5- or 6-membered heteroaryl ring containing one nitrogen atom and optionally 1-3 further heteroatoms chosen from oxygen, sulfur and nitrogen. Specific examples of such ring systems include, for example, indole, benzofuran, benzothiophene, benzimidazole, benzothiazole, benzisothiazole, benzoxazole, benzisoxazole, quinoline, quinoxaline, quinazoline, phthalazine and cinnoline.

Other particular examples of AR3 include 5/5-, 5/6 and 6/6 bicyclic ring systems containing heteroatoms in both of the rings. Specific examples of such ring systems include, for example, purine and naphthyridine.

Further particular examples of AR3 include bicyclic heteroaryl ring systems with at least one bridgehead nitrogen and optionally a further 1-3 heteroatoms chosen from oxygen, sulfur and nitrogen. Specific examples of such ring systems include, for example, 3H-pyrrolo[1,2-a]pyrrole, pyrrolo[2,1-b]thiazole, 1H-imidazo[1,2-a]pyrrole, 1H-imidazo[1,2-a]imidazole, 1H,3H-pyrrolo[1,2-c]oxazole, 1H-imidazo[1,5-a]pyrrole, pyrrolo[1,2-b]isoxazole, imidazo[5,1-b]thiazole, imidazo[2,1-b]thiazole, indolizine, imidazo[1,2-a]pyridine, imidazo[1,5-a]pyridine, pyrazolo[1,5-a]pyridine, pyrrolo[1,2-b]pyridazine, pyrrolo[1,2-c]pyrimidine, pyrrolo[1,2-a]pyrazine, pyrrolo[1,2-a]pyrimidine, pyrido[2,1-c]-s-triazole, s-triazole[1,5-a]pyridine, imidazo[1,2-c]pyrimidine, imidazo[1,2-a]pyrazine, imidazo[1,2-a]pyrimidine, imidazo[1,5-a]pyrazine, imidazo[1,5-a]pyrimidine, imidazo[1,2-b]-pyridazine, s-triazolo[4,3-a]pyrimidine, imidazo[5,1-b]oxazole and imidazo[2,1-b]oxazole. Other specific examples of such ring systems include, for example, [1H]-pyrrolo[2,1-c]oxazine, [3H]-oxazolo[3,4-a]pyridine, [6H]-pyrrolo[2,1-c]oxazine and pyrido[2,1-c][1,4]oxazine. Other specific examples of 5/5- bicyclic ring systems are imidazooxazole or imidazothiazole, in particular imidazo[5,1-b]thiazole, imidazo[2,1-b]thiazole, imidazo[5,1-b]oxazole or imidazo[2,1-b]oxazole.

Particular examples of AR3a and AR3b include, for example, indoline, 1,3,4,6,9,9a-hexahydropyrido[2,1c][1,4]oxazin-8-yl, 1,2,3,5,8,8a-hexahydroimidazo[1,5a]pyridin-7-yl, 1,5,8,8a-tetrahydrooxazolo[3,4a]pyridin-7-yl,

1,5,6,7,8,8a-hexahydrooxazolo[3,4a]pyridin-7-yl, (7aS)[3H,5H]-1,7a-dihydropyrrolo[1,2c]oxazol-6-yl, (7aS)[5H]-1,2,3,7a-tetrahydropyrrolo[1,2c]imidazol-6-yl, (7aR)[3H,5H]-1,7a-dihydropyrrolo[1,2c]oxazol-6-yl, [3H,5H]-pyrrolo[1,2-c]oxazol-6-yl, [5H]-2,3-dihydropyrrolo[1,2-c]imidazol-6-yl, [3H,5H]-pyrrolo[1,2-c]thiazol-6-yl, [3H,5H]-1,7a-dihydropyrrolo[1,2-c]thiazol-6-yl, [5H]-pyrrolo[1,2-c]imidazol-6-yl, [1H]-3,4,8,8a-tetrahydropyrrolo[2,1-c]oxazin-7-yl, [3H]-1,5,8,8a-tetrahydrooxazolo[3,4-a]pyrid-7-yl, [3H]-5,8-dihydroxazolo[3,4-a]pyrid-7-yl and 5,8-dihydroimidazo[1,5-a]pyrid-7-yl.

Particular values for AR4 include, for example, pyrrolo[a]quinoline, 2,3-pyrroloisoquinoline, pyrrolo[a]isoquinoline, 1H-pyrrolo[1,2-a]benzimidazole, 9H-imidazo[1,2-a]indole, 5H-imidazo[2,1-a]isoindole, 1H-imidazo[3,4-a]indole, imidazo[1,2-a]quinoline, imidazo[2,1-a]isoquinoline, imidazo[1,5-a]quinoline and imidazo[5,1-a]isoquinoline.

The nomenclature used is that found in, for example, "Heterocyclic Compounds (Systems with bridgehead nitrogen), W.L.Mosby (Interscience Publishers Inc., New York), 1961, Parts 1 and 2.

Where optional substituents are listed such substitution is preferably not geminal disubstitution unless stated otherwise. If not stated elsewhere suitable optional substituents for a particular group are those as stated for similar groups herein.

Suitable substituents on AR1, AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a and CY are (on an available carbon atom) up to three substituents independently selected from (1-4C)alkyl {optionally substituted by (preferably one) substituents selected independently from hydroxy, trifluoromethyl, (1-4C)alkyl $S(O)_q$- (q is 0, 1 or 2) (this last substituent preferably on AR1 only), (1-4C)alkoxy, (1-4C)alkoxycarbonyl, cyano, nitro, (1-4C)alkanoylamino, -CONRvRw or -NRvRw}, trifluoromethyl, hydroxy, halo, nitro, cyano, thiol, (1-4C)alkoxy, (1-4C)alkanoyloxy, dimethylaminomethyleneaminocarbonyl, di(N-(1-4C)alkyl)aminomethylimino, carboxy, (1-4C)alkoxycarbonyl, (1-4C)alkanoyl, (1-4C)alkylSO_2amino, (2-4C)alkenyl {optionally substituted by carboxy or (1-4C)alkoxycarbonyl}, (2-4C)alkynyl, (1-4C)alkanoylamino, oxo (=O), thioxo (=S), (1-4C)alkanoylamino {the (1-4C)alkanoyl group being optionally substituted by hydroxy}, (1-4C)alkyl $S(O)_q$- (q is 0, 1 or 2) {the (1-4C)alkyl group being optionally substituted by one or

more groups independently selected from cyano, hydroxy and (1-4C)alkoxy}, -CONRvRw or -NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl].

Further suitable substituents on AR1, AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a and CY (on an available carbon atom), and also on alkyl groups (unless indicated otherwise) are up to three substituents independently selected from trifluoromethoxy, benzoylamino, benzoyl, phenyl {optionally substituted by up to three substituents independently selected from halo, (1-4C)alkoxy or cyano}, furan, pyrrole, pyrazole, imidazole, triazole, pyrimidine, pyridazine, pyridine, isoxazole, oxazole, isothiazole, thiazole, thiophene, hydroxyimino(1-4C)alkyl, (1-4C)alkoxyimino(1-4C)alkyl, halo-(1-4C)alkyl, (1-4C)alkanesulfonamido, $-SO_2NRvRw$ [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl].

Preferable optional substituents on Ar2b as 1,3-dioxolan-4-yl, 1,3-dioxan-4-yl, 1,3-dioxan-5-yl or 1,4-dioxan-2-yl are mono- or disubstitution by substituents independently selected from (1-4C)alkyl (including geminal disubstitution), (1-4C)alkoxy, (1-4C)alkylthio, acetamido, (1-4C)alkanoyl, cyano, trifluoromethyl and phenyl].

Preferable optional substituents on CY are mono- or disubstitution by substituents independently selected from (1-4C)alkyl (including geminal disubstitution), hydroxy, (1-4C)alkoxy, (1-4C)alkylthio, acetamido, (1-4C)alkanoyl, cyano, and trifluoromethyl.

Suitable substituents on AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4 and AR4a are (on an available nitrogen atom, where such substitution does not result in quaternization) (1-4C)alkyl, (1-4C)alkanoyl {wherein the (1-4C)alkyl and (1-4C)alkanoyl groups are optionally substituted by (preferably one) substituents independently selected from cyano, hydroxy, nitro, trifluoromethyl, (1-4C)alkyl $S(O)_q$- (q is 0, 1 or 2), (1-4C)alkoxy, (1-4C)alkoxycarbonyl, (1-4C)alkanoylamino, -CONRvRw or -NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl]}, (2-4C)alkenyl, (2-4C)alkynyl, (1-4C)alkoxycarbonyl or oxo (to form an N-oxide).

For certain optional substituents suitable pharmaceutically-acceptable salts include acid addition salts such as methanesulfonate, fumarate, hydrochloride, citrate, maleate, tartrate and (less preferably) hydrobromide. Also suitable are salts formed with phosphoric and sulfuric acid. In another aspect suitable salts are base salts such as an alkali metal salt for example sodium, an alkaline earth metal salt for example calcium or magnesium, an organic amine salt for example triethylamine, morpholine, N-methylpiperidine, N-ethylpiperidine,

procaine, dibenzylamine, N,N-dibenzylethylamine, tris-(2-hydroxyethyl)amine, N-methyl D-glucamine and amino acids such as lysine. There may be more than one cation or anion depending on the number of charged functions and the valency of the cations or anions. A preferred pharmaceutically-acceptable salt is the sodium salt.

In addition certain salts of the sulfoximine NH residue are envisaged, by way of non - limiting example sulphonic acid derivatives, methane sulfonate, hydrochloride and hydrobromide salts.

However, to facilitate isolation of the salt during preparation, salts which are less soluble in the chosen solvent may be preferred whether pharmaceutically-acceptable or not.

The compounds of the formula (I) may be administered in the form of a pro-drug which is broken down in the human or animal body to give a compound of the formula (I). A prodrug may be used to alter or improve the physical and/or pharmacokinetic profile of the parent compound and can be formed when the parent compound contains a suitable group or substituent which can be derivatised to form a prodrug. Examples of pro-drugs include in-vivo hydrolysable esters of a compound of the formula (I) or a pharmaceutically-acceptable salt thereof.

Various forms of prodrugs are known in the art, for examples see:

a) Design of Prodrugs, edited by H. Bundgaard, (Elsevier, 1985) and Methods in Enzymology, Vol. 42, p. 309-396, edited by K. Widder, *et al.* (Academic Press, 1985);

b) A Textbook of Drug Design and Development, edited by Krogsgaard-Larsen and H. Bundgaard, Chapter 5 "Design and Application of Prodrugs", by H. Bundgaard p. 113-191 (1991);

c) H. Bundgaard, Advanced Drug Delivery Reviews, 8, 1-38 (1992);

d) H. Bundgaard, *et al.*, Journal of Pharmaceutical Sciences, 77, 285 (1988); and

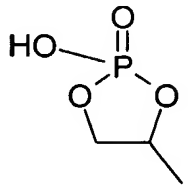
e) N. Kakeya, *et al.*, Chem Pharm Bull, 32, 692 (1984).

An in-vivo hydrolysable ester of a compound of the formula (I) or a pharmaceutically-acceptable salt thereof containing carboxy or hydroxy group is, for example, a pharmaceutically-acceptable ester which is hydrolysed in the human or animal body to produce the parent acid or alcohol. Suitable pharmaceutically-acceptable esters for carboxy include (1-6C)alkoxymethyl esters for example methoxymethyl, (1-6C)alkanoyloxymethyl esters for example pivaloyloxymethyl, phthalidyl esters, (3-8C)cycloalkoxycarbonyloxy(1-6C)alkyl esters for example 1-cyclohexylcarbonyloxyethyl; 1,3-dioxolan-2-onylmethyl esters

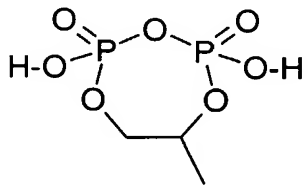
for example 5-methyl-1,3-dioxolan-2-ylmethyl; and (1-6C)alkoxycarbonyloxyethyl esters for example 1-methoxycarbonyloxyethyl and may be formed at any carboxy group in the compounds of this invention.

An in-vivo hydrolysable ester of a compound of the formula (I) or a pharmaceutically-acceptable salt thereof containing a hydroxy group or groups includes inorganic esters such as phosphate esters (including phosphoramidic cyclic esters) and α-acyloxyalkyl ethers and related compounds which as a result of the in-vivo hydrolysis of the ester breakdown to give the parent hydroxy group/s. In addition the sulphoximine residue may be derivatised by a convenient biologically labile group to give a derivative suitable for use as a solubilising pro-drug. Examples of α-acyloxyalkyl ethers include acetoxymethoxy and 2,2-dimethylpropionyloxymethoxy. A selection of in-vivo hydrolysable ester forming groups for hydroxy include (1-10C)alkanoyl, benzoyl, phenylacetyl and substituted benzoyl and phenylacetyl, (1-10C)alkoxycarbonyl (to give alkyl carbonate esters), di-(1-4C)alkylcarbamoyl and N-(di-(1-4C)alkylaminoethyl)-N-(1-4C)alkylcarbamoyl (to give carbamates), di-(1-4C)alkylaminoacetyl and carboxyacetyl. Examples of substituents on benzoyl and phenylacetyl include chloromethyl or aminomethyl, (1-4C)alkylaminomethyl and di-((1-4C)alkyl)aminomethyl, and morpholino or piperazino linked from a ring nitrogen atom via a methylene linking group to the 3- or 4-position of the benzoyl ring.

Certain suitable in-vivo hydrolysable esters of a compound of the formula (I) are described within the definitions listed in this specification, for example esters described by the definition (Rc2d), and some groups within (Rc2c). Suitable in-vivo hydrolysable esters of a compound of the formula (I) are described as follows. For example, a 1,2-diol may be cyclised to form a cyclic ester of formula (PD1) or a pyrophosphate of formula (PD2) :



(PD1)

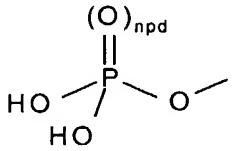


(PD2)

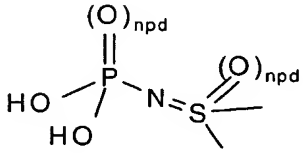
Particularly interesting are such cyclised pro-drugs when the 1,2-diol is on a (1-4C)alkyl chain linked to a carbonyl group in a substituent of formula Rc borne by a nitrogen atom in structures (TA1) or (TA2). Esters of compounds of formula (I) wherein the HO-function/s in (PD1) and (PD2) are protected by (1-4C)alkyl, phenyl or benzyl are useful

intermediates for the preparation of such pro-drugs.

Further in-vivo hydrolysable esters include phosphoramidic esters, and also compounds of formula (I) in which any free hydroxy group, or sulfoxime group, independently forms a phosphoryl (npd is 1) or phosphiryl (npd is 0) ester of the formula (PD3) or (PS1), wherein npd is independently 0 or 1 for each oxo group :



(PD3)



(PS1)

For the avoidance of doubt, phosphono is $-P(O)(OH)_2$; (1-4C)alkoxy(hydroxy)-phosphoryl is a mono-(1-4C)alkoxy derivative of $-O-P(O)(OH)_2$; and di-(1-4C)alkoxyphosphoryl is a di-(1-4C)alkoxy derivative of $-O-P(O)(OH)_2$.

Useful intermediates for the preparation of such esters include compounds containing a group/s of formula (PD3) in which either or both of the -OH groups in (PD3) is independently protected by (1-4C)alkyl (such compounds also being interesting compounds in their own right), phenyl or phenyl-(1-4C)alkyl (such phenyl groups being optionally substituted by 1 or 2 groups independently selected from (1-4C)alkyl, nitro, halo and (1-4C)alkoxy).

Thus, prodrugs containing groups such as (PD1), (PD2) and (PD3) may be prepared by reaction of a compound of formula (I) containing suitable hydroxy group/s with a suitably protected phosphorylating agent (for example, containing a chloro or dialkylamino leaving group), followed by oxidation (if necessary) and deprotection. Prodrugs containing a group such as (PS1) may be obtained by analogous chemistry.

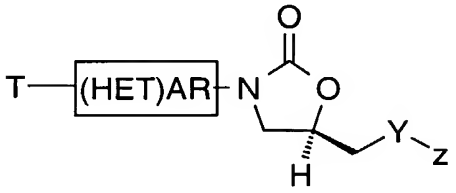
When a compound of formula (I) contains a number of free hydroxy group, those groups not being converted into a prodrug functionality may be protected (for example, using a t-butyl-dimethylsilyl group), and later deprotected. Also, enzymatic methods may be used to

selectively phosphorylate or dephosphorylate alcohol functionalities.

Other interesting in-vivo hydrolysable esters include, for example, those in which Rc is defined by, for example, $R^{14}C(O)O(1\text{-}6C)alkyl\text{-}CO\text{-}$ (wherein R^{14} is for example, benzyloxy-(1-4C)alkyl, or phenyl). Suitable substituents on a phenyl group in such esters include, for example, 4-(1-4C)piperazino-(1-4C)alkyl, piperazino-(1-4C)alkyl and morpholino-(1-4C)alkyl.

Where pharmaceutically-acceptable salts of an in-vivo hydrolysable ester may be formed this is achieved by conventional techniques. Thus, for example, compounds containing a group of formula (PD1), (PD2) and/or (PD3) may ionise (partially or fully) to form salts with an appropriate number of counter-ions. Thus, by way of example, if an in-vivo hydrolysable ester prodrug of a compound of formula (I) contains two (PD3) groups, there are four HO-P- functionalities present in the overall molecule, each of which may form an appropriate salt (i.e. the overall molecule may form, for example, a mono-, di-, tri- or tetra-sodium salt).

The compounds of the present invention have a chiral centre at the C-5 position of the oxazolidinone ring. The pharmaceutically active enantiomer is of the formula (I):



(I)

The present invention includes the pure enantiomer depicted above or mixtures of the R and S enantiomers, for example a racemic mixture. If a mixture of enantiomers is used, a larger amount (depending upon the ratio of the enantiomers) will be required to achieve the same effect as the same weight of the pharmaceutically active enantiomer. For the avoidance of doubt the enantiomer depicted above is the R enantiomer.

Furthermore, the compounds of the formula (I) may have other chiral centres, for example certain sulfoxime compounds may be chiral at the sulfur atom. It is to be understood that the invention encompasses all such optical and diastereo-isomers, and racemic mixtures, that possess antibacterial activity. It is well known in the art how to prepare optically-active forms (for example by resolution of the racemic form by recrystallisation techniques, by chiral

synthesis, by enzymatic resolution, by biotransformation or by chromatographic separation) and how to determine antibacterial activity as described hereinafter.

Furthermore, some compounds of the formula (I), for example certain sulfoxime compounds may exist as cis- and trans-isomers. It is to be understood that the invention encompasses all such isomers, and mixtures thereof, that possess antibacterial activity.

The invention relates to all tautomeric forms of the compounds of the formula (I) that possess antibacterial activity.

It is also to be understood that certain compounds of the formula (I) can exist in solvated as well as unsolvated forms such as, for example, hydrated forms. It is to be understood that the invention encompasses all such solvated forms which possess antibacterial activity.

It is also to be understood that certain compounds of the formula (I) may exhibit polymorphism, and that the invention encompasses all such forms which possess antibacterial activity.

As stated before, we have discovered a range of compounds that have good activity against a broad range of Gram-positive pathogens including organisms known to be resistant to most commonly used antibiotics, together with activity against fastidious Gram negative pathogens such as H.influenzae and M.catarrhalis, Mycoplasma and Chlamydia strains.They have good physical and/or pharmacokinetic properties in general, and favourable toxicological profiles.

Particularly preferred compounds of the invention comprise a compound of formula (I), or a pharmaceutically-acceptable salt or an in-vivo hydrolysable ester thereof, wherein the substituents HET, T and other substituents mentioned above have values disclosed hereinbefore, or any of the following values (which may be used where appropriate with any of the definitions and embodiments disclosed hereinbefore or hereinafter):

In one embodiment of the invention are provided compounds of formula (I), in an alternative embodiment are provided pharmaceutically-acceptable salts of compounds of formula (I), and in a further alternative embodiment are provided in-vivo hydrolysable esters of compounds of formula (I).

In one embodiment is provided a compound of formula (I) as defined herein, or pharmaceutically-acceptable salt or in-vivo hydrolysable ester thereof, wherein T is selected from (TA2) and (TB). In another embodiment is provided a compound of formula (I) as

defined herein, or a pharmaceutically-acceptable salt or in-vivo hydrolysable ester thereof, wherein T is (TA1). In a further embodiment is provided a compound of formula (I) as defined herein, or a pharmaceutically-acceptable salt or in-vivo hydrolysable ester thereof, wherein T is (TA1b).

In a further embodiment is provided a compound of formula (I) as defined herein, or a pharmaceutically-acceptable salt or in-vivo hydrolysable ester thereof, wherein T is selected from (TA1), (TA2) and (TB) and wherein when T is (TA1) the ring contains one of :

(i) one double bond between any two ring carbon atoms; or

(ii) a C1-C3 bridge connecting any two appropriate, non-adjacent ring carbon atoms, which bridge may optionally contain one heteroatom selected from oxygen or >NRc; or

(iii) a C2-C5 cyclic moiety including a ring carbon atom to define a spiro C2-C5 ring system, which ring may optionally contain one heteroatom selected from oxygen or >NRc; or

(iv) a C1-C4 bridge connecting adjacent carbon atoms to define a fused ring, wherein a C2-C4 bridge may optionally contain one heteroatom selected from oxygen or >NRc; wherein Rc is as defined hereinbefore or hereinafter;

and wherein when T is (TA2), $()n_1$ and $()o_1$ are independently 0, 1 or 2 and represent chains of carbon atoms (optionally substituted as defined for AR1) of length n_1 and o_1 respectively, and define a 4- to 8-membered monocyclic ring, which ring contains one of

(i) a C1-C3 bridge connecting any two appropriate, non-adjacent ring carbon atoms, which bridge contains one heteroatom selected from oxygen or >NRc; or

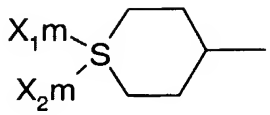
(ii) a C2-C5 cyclic moiety including a ring carbon atom to define a spiro C2-C5 ring system, which ring may optionally contain one heteroatom selected from oxygen or >NRc; or

(iii) a C1-C4 bridge connecting adjacent carbon atoms to define a fused ring, wherein a C2-C4 bridge may optionally contain one heteroatom selected from oxygen or >NRc; wherein Rc is as defined hereinbefore or hereinafter;

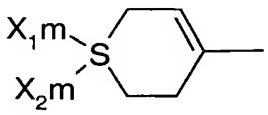
and wherein when T is (TB), T may not be (TB1b) .

In (TA1), when the ring has an optional double bond between any two ring carbon atoms, the ring is preferably linked via an sp^2 carbon atom of the double bond.

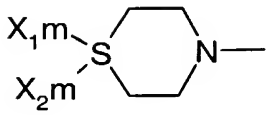
Preferably (TA1) is (TA1a) or (TA1b), and preferably (TA2) is (TA2a) :-



(TA1a)



(TA1b)

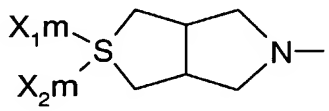


(TA2a)

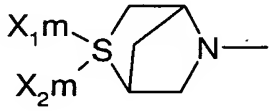
wherein X_{1m} and X_{2m} are as defined above, and hereinafter.

More preferably (TA1) is (TA1b).

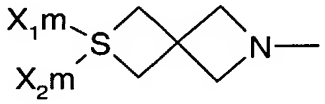
In (TB1) to (TB3), preferably $n_1 = o_1$ & $n_{1'} = o_{1'}$ (most preferably all are 1); $p_1 = p_{1'}$ (most preferably both are 0); and further preferred values for the groups defined in (TB) are defined by formulae (TB1a, b), (TB2a) and (TB3a) :-



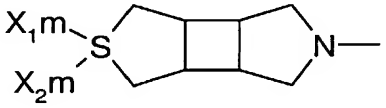
(TB1a)



(TB1b)



(TB2a)



(TB3a)

wherein X_{1m} and X_{2m} are as defined above, and hereinafter.

When (TA) is (TA1a) or (TA2a), preferably X_{1m} and X_{2m} together are represent R_{2s}-$(E)_{ms}$-N=, wherein R_{2s} and -$(E)_{ms}$ are as defined above, and hereinafter.

When (TB) is (TB1b) preferably X_{1m} and X_{2m} together are represent R_{2s}-$(E)_{ms}$-N=, wherein R_{2s} and -$(E)_{ms}$ are as defined above, and hereinafter.

In one embodiment, preferably X_{1m} is O= and X_{2m} is R_{2s}-$(E)_{ms}$-N-, and vice versa. In another embodiment, preferably X_{1m} and X_{2m} together are represent R_{2s}-$(E)_{ms}$-N=; wherein in either embodiment, R_{2s} and -$(E)_{ms}$ are as defined above, and hereinafter.

When ms is 0, R_{2s} is preferably selected from :

(i) hydrogen, a (1-6C)alkyl group {optionally monosubstituted by (1-4C)alkanoyl group, cyano, cyano-imino, (1-4C)alkoxy, trifluoromethyl, (1-4C)alkoxycarbonyl, phenyl (optionally substituted as for AR1 defined herein), optionally substituted heteroaryl group of the formula AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a or CY all as defined (and optionally substituted as defined) herein, (1-4C)alkylS(O)$_q$- (q is 0, 1 or 2); or optionally substituted by one or more fluoro groups (including geminal disubstitution); or optionally substituted by one

or more hydroxy groups (excluding geminal disubstitution), and/or optionally further substituted, by no more than one of each of, oxo, -NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl], (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino, N-(1-4C)alkyl-N-(1-6C)alkanoylamino, (1-4C)alkylS(O)$_p$NH- or (1-4C)alkylS(O)$_p$-((1-4C)alkyl)N- (p is 1 or 2)}; or

(ii) an optionally substituted aryl or optionally substituted heteroaryl group of the formula AR1, AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a or CY all as defined (and optionally substituted as defined) herein; or

(iii) cyano, -CO-NRvRw, -CO-NRv Rw', -SO_2-NRvRw, -SO_2-NRv Rw' [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl; Rw' is phenyl (optionally substituted as for AR1 defined herein), or a heteroaryl group selected from AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a (optionally substituted as defined herein)], (1-4C)alkoxycarbonyl, trifluoromethyl.

When ms is 0, R_{2s} is most preferably selected from :

(i) hydrogen, (1-6C)alkyl {optionally monosubstituted by (1-4C)alkoxy, trifluoromethyl, (1-4C)alkylS(O)$_q$- (q is 0, 1 or 2); or optionally substituted by one or more fluoro-groups (including geminal disubstitution); or optionally substituted by one or more hydroxy groups (excluding geminal disubstitution)}; or

(iii) -CO-NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl], -CO-NRv Rw' [wherein Rv is hydrogen or (1-4C)alkyl; Rw' is phenyl (optionally substituted as for AR1 defined herein)], (1-4C)alkoxycarbonyl.

When ms is 1, E is preferably -CO- or -SO_2- and R_{2s} is preferably selected from :

(i) (1-6C)alkyl {optionally monosubstituted by cyano, cyano-imino, (1-4C)alkoxy, trifluoromethyl, (1-4C)alkoxycarbonyl, phenyl (optionally substituted as for AR1 defined herein), optionally substituted heteroaryl group of the formula AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a or CY all as defined (and optionally substituted as defined) herein, (1-4C)alkylS(O)$_q$- (q is 0, 1 or 2); and/or (with the proviso that where R_{2s} is -SO_2- or -O-CO- not on the first carbon atom of the (1-6C) alkyl chain) optionally substituted by one or more groups (including geminal disubstitution) each independently selected from hydroxy and fluoro, and/or optionally monosubstituted by -NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl], (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino, N-(1-4C)alkyl-N-(1-6C)alkanoylamino, (1-4C)alkylS(O)$_p$NH- or (1-4C)alkylS(O)$_p$-((1-

4C)alkyl)N- (p is 1 or 2)}; or

(ii) an optionally substituted aryl or heteroaryl group of the formula AR1, AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a or CY all as defined (and optionally substituted as defined) herein.

When ms is 1, E is preferably -CO- or -SO_2- and R_{2s} is most preferably selected from :

(i) (1-6C)alkyl {optionally monosubstituted by (1-4C)alkoxy, trifluoromethyl, (1-4C)alkylS(O)$_q$- (q is 0, 1 or 2); or optionally substituted by one or more fluoro groups (including geminal disubstitution); or optionally substituted by one or more hydroxy groups (excluding geminal disubstitution)}, (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino.

In (TB) and (TA2), where ()n_1, ()o_1, ()$n_{1'}$, ()$o_{1'}$, ()p_1 and ()$p_{1'}$ represent chains of carbon atoms optionally substituted as defined for AR1 herein, preferable optional substituents are selected from (preferably one of) hydroxy, trifluoromethyl, (1-4C)alkyl S(O)$_q$- (q is 0, 1 or 2), (1-4C)alkoxy, (1-4C)alkoxycarbonyl, cyano, nitro, (1-4C)alkanoylamino, -CONRvRw or –NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl]. Most preferably, ()n_1, ()o_1, ()$n_{1'}$, ()$o_{1'}$, ()p_1 and ()$p_{1'}$ represent unsubstituted chains of carbon atoms.

Preferable values for other substituents (which may be used where appropriate with any of the definitions and embodiments disclosed hereinbefore or hereinafter) are :-

(a) In one embodiment, HET(AR) is a 5 membered aromatic or heteroaromatic ring as defined herein and optionally substituted as defined herein. In another embodiment HET(AR) is a 6 membered aromatic or heteroaromatic ring as defined herein and optionally substituted as defined herein. Preferably HET(AR) is phenyl. In a further embodiment, HET(AR) is not phenyl.

(b) In one aspect preferably HET(AR) is substituted at both positions ortho to the carbon atom on the adjacent sulfilimine/sulfoximine ring by R1 as defined herein. In an another aspect HET(AR) is substituted at one such position.

(c) Preferably R1 is hydrogen or halogen. Most preferably R1 is hydrogen or fluorine.

(d) In one embodiment, preferably Y is NH. In another embodiment, preferably Y is (1-6C)alkyl or –COOR5 wherein R5 is as hereinbefore defined.

(e) In one embodiment, preferably Z is a 5 membered heteroaromatic ring joined to Y via a ring carbon atom. Preferably Z is isoxazol-3-yl. In another embodiment, preferably Z is a 6 membered heteroaromatic ring.

(f) Preferably Rc is R^{13}CO- and preferably R^{13} is (1-4C)alkoxycarbonyl,

hydroxy(1-4C)alkyl, (1-4C)alkyl (optionally substituted by one or two hydroxy groups, or by an (1-4C)alkanoyl group), (1-4C)alkylamino, dimethylamino(1-4C)alkyl, (1-4C)alkoxymethyl, (1-4C)alkanoylmethyl, (1-4C)alkanoyloxy(1-4C)alkyl, (1-5C)alkoxy or 2-cyanoethyl.

(g) More preferably R^{13} is 1,2-dihydroxyethyl, 1,3-dihydroxyprop-2-yl, 1,2,3-trihydroxyprop-1-yl, methoxycarbonyl, hydroxymethyl, methyl, methylamino, dimethylaminomethyl, methoxymethyl, acetoxymethyl, methoxy, methylthio, naphthyl, tert-butoxy or 2-cyanoethyl.

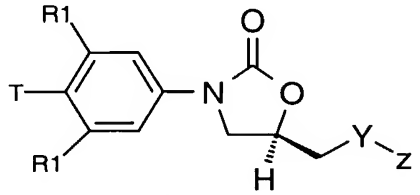
(h) Particularly preferred as R^{13} is 1,2-dihydroxyethyl, 1,3-dihydroxyprop-2-yl or 1,2,3-trihydroxyprop-1-yl.

(i) In another aspect preferably R^{13} is hydrogen, (1-10C)alkyl [optionally substituted by one or more hydroxy] or $R^{14}C(O)O(1\text{-}6C)alkyl$.

For compounds of formula (I) preferred values for Rc are those in group (Rc2) when present in any of the definitions herein containing Rc.

In the definition of (Rc2c) the AR2a, AR2b, AR3a and AR3b versions of AR2 and AR3 containing groups are preferably excluded.

Especially preferred compounds of the present invention are of the formula (1B):



(IB)

wherein Y is NH and Z is isoxazol-3-yl; each R_1 is independently hydrogen or fluoro; T is selected from (TA1), (TA2) and (TB1) to (TB3) wherein X_{1m} and X_{2m} together represent R_{2s}-$(E)_{ms}$-N= (as defined hereinbefore or hereinafter); or in-vivo hydrolysable esters or pharmaceutically acceptable salts thereof.

Further especially preferred compounds of the invention are of the formula (IB) wherein Y is NH and Z is isoxazol-3-yl; each R_1 is independently hydrogen or fluoro; T is (TA1b); wherein X_{1m} is O= and X_{2m} is R_{2s}-$(E)_{ms}$-N-, and vice versa (as defined hereinbefore or hereinafter); or in-vivo hydrolysable esters or pharmaceutically acceptable salts thereof.

Further especially preferred compounds of the invention are of the formula (IB) wherein Y is NH and Z isoxazol-3-yl; each R_1 is independently hydrogen or fluoro; T is

selected from TB1 to TB3 (but excluding (TB1b)) wherein X_{1m} is O= and X_{2m} is R_{2s}-$(E)_{ms}$-N-, and vice versa (as defined hereinbefore or hereinafter); or in-vivo hydrolysable esters or pharmaceutically acceptable salts thereof.

Further especially preferred compounds of the invention are of the formula (IB) wherein Y is -NR4- (wherein R4 is (1-6C)alkyl or –COOR5 (wherein R5 is as hereinbefore defined)) and Z is isoxazol-3-yl; each R_1 is independently hydrogen or fluoro; T is (TA1b); wherein X_{1m} is O= and X_{2m} is R_{2s}-$(E)_{ms}$-N-, and vice versa (as defined hereinbefore or hereinafter); or in-vivo hydrolysable esters or pharmaceutically acceptable salts thereof.

In the above aspects and preferred compounds of formula (IB), in (TA1), (TA2) and (TB1) to (TB3) when ms is 0, R_{2s} is preferably selected from

(i) hydrogen, a (1-6C)alkyl group {optionally monosubstituted by (1-4C)alkanoyl group, cyano, cyano-imino, (1-4C)alkoxy, trifluoromethyl, (1-4C)alkoxycarbonyl, phenyl (optionally substituted as for AR1 defined herein), optionally substituted heteroaryl group of the formula AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a or CY all as defined (and optionally substituted as defined) herein, (1-4C)alkylS(O)$_q$- (q is 0, 1 or 2); or optionally substituted by one or more fluoro groups (including geminal disubstitution); or optionally substituted by one or more hydroxy groups (excluding geminal disubstitution), and/or optionally further substituted, by no more than one of each of, oxo, -NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl], (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino, N-(1-4C)alkyl-N-(1-6C)alkanoylamino, (1-4C)alkylS(O)$_p$NH- or (1-4C)alkylS(O)$_p$-((1-4C)alkyl)N- (p is 1 or 2)}; or

(ii) an optionally substituted aryl or optionally substituted heteroaryl group of the formula AR1, AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a or CY all as defined (and optionally substituted as defined) herein;

or (where ms is 0 only),

(iii) cyano, -CO-NRvRw, -CO-NRv Rw', -SO_2-NRvRw, -SO_2-NRv Rw' [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl; Rw' is phenyl (optionally substituted as for AR1 defined herein), or a heteroaryl group selected from AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a (optionally substituted as defined herein)],

(1-4C)alkoxycarbonyl, trifluoromethyl;

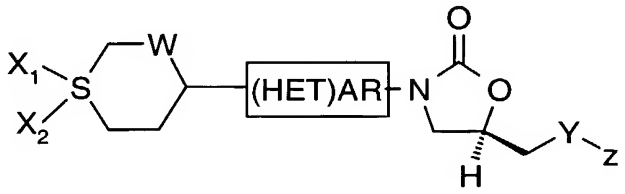
and when ms is 1, E is preferably -CO- or -SO_2- and R_{2s} is preferably selected from :

(i) (1-6C)alkyl {optionally monosubstituted by cyano, cyano-imino, (1-4C)alkoxy,

trifluoromethyl, (1-4C)alkoxycarbonyl, phenyl (optionally substituted as for AR1 defined herein), optionally substituted heteroaryl group of the formula AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a or CY all as defined (and optionally substituted as defined) herein, (1-4C)alkylS(O)$_q$- (q is 0, 1 or 2); and/or (with the proviso that where R_{2s} is -SO_2- or -O-CO- not on the first carbon atom of the (1-6C) alkyl chain) optionally substituted by one or more groups (including geminal disubstitution) each independently selected from hydroxy and fluoro, and/or optionally monosubstituted by -NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl], (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino, N-(1-4C)alkyl-N-(1-6C)alkanoylamino, (1-4C)alkylS(O)$_p$NH- or (1-4C)alkylS(O)$_p$-((1-4C)alkyl)N- (p is 1 or 2)}; or

(ii) an optionally substituted aryl or heteroaryl group of the formula AR1, AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a or CY all as defined (and optionally substituted as defined) herein.

In a further aspect of the invention, is provided a compound of formula (I) wherein T is (TA1) as hereinbefore defined; and therefore provides a compound of the formula (IC), or a pharmaceutically-acceptable salt, or an in-vivo-hydrolysable ester thereof,



(IC)

wherein:

X1 and **X2** taken together represent $R2_F$-(E)m-N=, wherein E is an electron withdrawing group selected from SO2-, CO-, O-CO-, CO-O-, CS-, CON(R_F)-, SO2N(R_F)-, or E may represent a group of the formula $R3_F$ -C(=N-O-$R3_F$)-C(=O)-, wherein $R3_F$ is H or as defined in $R2_F$ (i) below; or

X1 is O= and **X2** is $R2_F$ -(E)m-N-, and vice versa;

and $R2_F$ and R_F may be linked as a 5- or 6-membered unsaturated or partially unsaturated ring;

m is 0 or 1;

$R2_F$ and **R_F** are independently selected from:

(i) hydrogen (except where E is SO2 or O-CO-), a (1-6C)alkyl group {optionally substituted by one or more (1-4C)alkanoyl groups (including geminal disubstitution) and/or optionally monosubstituted by cyano, (1-4C)alkoxy, trifluoromethyl, (1-4C)alkoxycarbonyl, phenyl (optionally substituted as for AR defined herein after, heteroaryl(optionally substituted and defined as below),(1-4C)alkylS(O)$_q$- (q is 0, 1 or 2); or (with the proviso that where R2$_F$ is SO2 or O-CO- not on the first carbon atom of the (1-6C) alkyl chain) optionally substituted by one or more groups (including geminal disubstitution) each independently selected from hydroxy and fluoro, and/or optionally monosubstituted by oxo, -NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl], (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino, N-(1-4C)alkyl-N-(1-6C)alkanoylamino, (1-4C)alkylS(O)$_p$NH- or (1-4C)alkylS(O)$_p$-((1-4C)alkyl)N- (p is 1 or 2)};

or

(ii) an optionally substituted aryl or heteroaryl group of the formula AR1, AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a, or CY all as hereinbefore defined,

or where m=0 only,

(iii) cyano (1-4C)alkoxycarbonyl, trifluoromethyl, ethenyl, 2-(1-4C)alkylethenyl, 2-cyanoethenyl, 2-cyano-2-((1-4C)alkyl)ethenyl, 2-nitroethenyl, 2-nitro-2-((1-4C)alkyl)ethenyl, 2-((1-4C)alkylaminocarbonyl)ethenyl, 2-((1-4C)alkoxycarbonyl)ethenyl, 2-(AR1)ethenyl, 2-(AR2)ethenyl, or 2-(AR2a)ethenyl;

W is a bond joining the adjacent carbon atoms or represents one or two carbon atoms (each -CH2- or -CH-), the heterocyclic ring comprising W therefore has 5-7 ring atoms and may optionally have one or more of (i) one double bond between ring carbon atoms, (ii) a C1-C3 bridge connecting two ring carbon atoms and optionally containing a heteroatom selected from oxygen or nitrogen, and (iii) a C2-C5 cyclic moiety around a ring carbon atom;

(HET)AR is a 5-6 membered aromatic or heteroaromatic ring, (i) when a 5-membered ring this may be a thiophene ring, comprising a single sulphur atom sited ortho to the nitrogen atom on the adjacent oxazolidinone ring, such a ring may have a single optional substituent R1$_F$ as hereinafter defined sited ortho to the carbon atom on the adjacent sulfilimine/sulfoximine ring, (ii) when a 6-membered ring this may be a phenyl ring or comprise a single nitrogen atom sited ortho to the nitrogen atom on the adjacent oxazolidinone ring, such ring may be optionally substituted at one or both positions ortho to the carbon atom on the adjacent sulfilimine/sulfoximine ring by R1$_F$, where each

$R1_F$ is independently selected from hydrogen, halogen, methyl, methoxy, ethyl and ethoxy;

Y is -NR4- wherein R4 is hydrogen, or (1-6C)alkyl or -COOR5 wherein R5 is (1-6C)alkyl optionally substituted by one or more chlorine atoms;

Z is a C5-C6 heteroaromatic ring joined to Y via a ring carbon atom, which ring is optionally substituted on an available carbon atom by 1 or 2 substituents independently selected from (1-4C)alkyl, amino, (1-4C)alkylamino, (1-4C)alkoxy and halogen, and/or on an available nitrogen atom (provided that the ring is not thereby quaternised) by (1-4C)alkyl;

except that (other than when the heterocyclic ring comprising M is optionally substituted as defined in (i) – (iii) above), when X_1 is O= and X_2 is $R2_F$-(E)m-N-, or vice versa, $R2_F$-(E)m- may not be hydrogen, (1-4C)alkyl (optionally substituted as defined for R_p below), -C(=O)(1-4C)alkyl (optionally substituted as defined for R_p below), -C(=O)O(1-4C)alkyl (optionally substituted as defined for R_p below), -C(=O)NHR$_p$, or –C(=S)NHR$_p$,

wherein R_p is hydrogen, (1-4C)alkyl (optionally substituted with one or more halo, cyano, nitro, phenyl, (3-6C)cycloalkyl, OR_{p2}, $C(=O)R_{p2}$, $OC(=O)R_{p2}$, $C(=O)OR_{p2}$, $S(=O)_{mp}R_{p2}$, $S(=O)_{mp}NR_{p2}R_{p2}$, $NR_{p2}SO_2R_{p2}$, $NR_{p2}NSO_2R_{p2}R_{p2}$, $NR_{p2}C(=O)R_{p2}$, $C(=O)NR_{p2}R_{p2}$, $NR_{p2}R_{p2}$, oxo or oxime) or phenyl,

wherein R_{p2} is hydrogen, (1-4C)alkyl or phenyl,

wherein at each occurrence phenyl is optionally substituted with one or more halo, cyano, nitro, phenyl, (3-6C)cycloalkyl, OR_{p2}, $C(=O)R_{p2}$, $OC(=O)R_{p2}$, $C(=O)OR_{p2}$, $S(=O)_{mp}R_{p2}$, $S(=O)_{mp}NR_{p2}R_{p2}$, $NR_{p2}SO_2R_{p2}$, $NR_{p2}NSO_2R_{p2}R_{p2}$, $NR_{p2}C(=O)R_{p2}$, $C(=O)NR_{p2}R_{p2}$, or $NR_{p2}R_{p2}$,

mp is 0, 1 or 2;

For compounds of the formula (IC) the term "a C5-C6 heteroaromatic ring" means a 5- or 6-membered aryl ring wherein (unless stated otherwise) 1, 2 or 3 of the ring atoms are selected from nitrogen, oxygen and sulfur. Unless stated otherwise, such rings are fully aromatic. Particular examples of 5- or 6-membered heteroaryl ring systems are furan, pyrrole, pyrazole, imidazole, triazole, pyrimidine, pyridazine, pyridine, isoxazole, oxazole, isothiazole, thiazole and thiophene.

For compounds of the formula (IC), particular optional substituents for alkyl, phenyl (and phenyl containing moieties) and naphthyl groups and ring carbon atoms in heteroaryl (mono or bicyclic) rings (such as set out hereinbefore in groups AR1 to AR4a and CY

inclusive) include halo, (1-4C)alkyl , hydroxy, nitro, carbamoyl, (1-4C)alkylcarbamoyl, di-((1-4C)alkyl)carbamoyl, cyano, trifluoromethyl, trifluoromethoxy, amino, (1-4C)alkylamino, di((1-4C)alkyl)amino, (1-4C)alkyl $S(O)_q$- (q is 0, 1 or 2), carboxy, (1-4C)alkoxycarbonyl, (2-4C)alkenyl, (2-4C)alkynyl, (1-4C)alkanoyl, (1-4C)alkoxy, (1-4C)alkyl$S(O)_2$amino, (1-4C)alkanoylamino, benzoylamino, benzoyl, phenyl (optionally substituted by up to three substituents selected from halo, (1-4C)alkoxy or cyano), furan, pyrrole, pyrazole, imidazole, triazole, pyrimidine, pyridazine, pyridine, isoxazole, oxazole, isothiazole, thiazole, thiophene, hydroxyimino(1-4C)alkyl, (1-4C)alkoxyimino(1-4C)alkyl, hydroxy-(1-4C)alkyl, halo-(1-4C)alkyl, nitro(1-4C)alkyl, amino(1-4C)alkyl, cyano(1-4C)alkyl, (1-4C)alkanesulfonamido, aminosulfonyl, (1-4C)alkylaminosulfonyl and di-((1-4C)alkyl)aminosulfonyl. The phenyl and naphthyl groups and heteroaryl (mono- or bicyclic) rings may be mono- or di-substituted on ring carbon atoms with substituents independently selected from the above list of particular optional substituents, or on ring nitrogen atoms provided the ring is not thereby quaternised.

AR1, AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a and CY are understood to be as hereinbefore defined for formula I.

Particular values for **X1** and **X2** are as follows:

(i) X1 is O= and X2 is $R2_F$ -(E)m-N-, wherein m = 0 and vice versa,

(ii) X1 is O= and X2 is $R2_F$ -(E)m-N-, wherein m is 1 and vice versa

(iii) X1 and X2 taken together represent $R2_F$ -(E)m-N=, wherein E is -SO2- and m is 0

(iv) X1 and X2 taken together represent $R2_F$ -(E)m-N=, wherein E is -SO2- and m is 1

(v) X1 and X2 taken together represent $R2_F$ -(E)m-N=, wherein E is -CO- and m is 0

(vi) X1 and X2 taken together represent $R2_F$ -(E)m-N=, wherein E is -CO- and m is 1

(vii) X1 and X2 taken together represent $R2_F$ -(E)m-N=, wherein E is -O-CO- and m is 0

(viii) X1 and X2 taken together represent $R2_F$ -(E)m-N=, wherein E is -O-CO- and m is 1

(ix) X1 and X2 taken together represent $R2_F$ -(E)m-N=, wherein E is -CO-O- and m is 0

(x) X1 and X2 taken together represent $R2_F$ -(E)m-N=, wherein E is -COO-- and m is 1

(xi) X1 and X2 taken together represent $R2_F$ -(E)m-N=, wherein E is -CS- and m is 0

(xii) X1 and X2 taken together represent $R2_F$ -(E)m-N=, wherein E is -CS- and m is 1

(xiii) X1 and X2 taken together represent $R2_F$ -(E)m-N=, wherein E is -CON(R_F)- and m is 0

(xiv) X1 and X2 taken together represent $R2_F$ -(E)m-N=, wherein E is -CON(R_F)- and m is 1

(xv) X1 and X2 taken together represent $R2_F$ -(E)m-N=, wherein E is -SO2N(R_F)- and m is 0

(xvi) X1 and X2 taken together represent $R2_F$ -(E)m-N=, wherein E is -SO2N(R_F)- and m is 1;

$R1_F$ is hydrogen or halogen;

$R2_F$ and **R_F** are independently hydrogen (except where E is SO2 or O-CO-), a (1-6C)alkyl group {optionally substituted by one or more (1-4C)alkanoyl groups (including geminal disubstitution) and/or optionally monosubstituted by cyano, (1-4C)alkoxy, trifluoromethyl, (1-4C)alkoxycarbonyl, phenyl (optionally substituted as for AR defined hereinafter, heteroaryl(optionally substituted and defined as below),(1-4C)alkylS(O)$_q$- (q is 0, 1 or 2); oroptionally substituted by one or more groups (including geminal disubstitution) each independently selected from hydroxy and fluoro, and/or optionally monosubstituted by oxo, -NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl], (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino, N-(1-4C)alkyl-N-(1-6C)alkanoylamino, (1-4C)alkylS(O)$_p$NH- or (1-4C)alkylS(O)$_p$-((1-4C)alkyl)N- (p is 1 or 2)};

m is 1

Y is -NH- or -protected amino-;

Z is a 5-membered heterocyclic ring;

the optional double bond in the heterocyclic ring comprising W is adjacent to the bond linking the heterocyclic ring to the ring (HET)AR.

More particular values are as follows:

E is absent or is SO2-;

$R1_F$ is halogen;

$R2_F$ and **R_F** are independently hydrogen (except where E is SO2 or O-CO-), an alkyl, cycloalkyl, alkenyl or alkynyl group [especially cyclopropyl, or cyclobutyl, ethyl or methyl], all being optionally substituted by one or more of hydroxy, O-alkyl, alkanoyl (including geminal disubstitution), CN, SO2CH3, fluorine, chlorine, trifluoromethyl, COOH, COO-alkyl, CONH2, CONH-alkyl, or CON-dialkyl; and wherein any group has up to 6, such as up to 4 carbon atoms, the O-alkyl and alkanoyl groups may be further substituted by any convenient substituent such as for example trifluoromethyl;

Y is NH;

Z is isoxazol-3-yl.

In all of the above aspects and preferred compounds of formula (IB) and (IC), in-vivo hydrolysable esters are preferred where appropriate, especially phosphoryl esters (as defined by formula (PD3) with npd as 1, or of formula (PS1)).

In all of the above definitions the preferred compounds are as shown in formula (I), ie the pharmaceutically active enantiomer.

Particularly preferred compounds of the present invention include the compounds described in the following examples. Therefore the present invention also provides a compound described in any one of the following examples, or a pharmaceutically-acceptable salt or an in-vivo hydrolysable ester thereof (and in particular compounds and salts thereof); and their use as a medicament (as herein described).

Process section:

In a further aspect the present invention provides a process for preparing a compound of formula (I) or a pharmaceutically-acceptable salt or an in-vivo hydrolysable ester thereof. It will be appreciated that during certain of the following processes certain substituents may require protection to prevent their undesired reaction. The skilled chemist will appreciate when such protection is required, and how such protecting groups may be put in place, and later removed.

For examples of protecting groups see one of the many general texts on the subject, for example, 'Protective Groups in Organic Synthesis' by Theodora Green (publisher: John Wiley & Sons). Protecting groups may be removed by any convenient method as described in the literature or known to the skilled chemist as appropriate for the removal of the protecting group in question, such methods being chosen so as to effect removal of the protecting group with minimum disturbance of groups elsewhere in the molecule.

Thus, if reactants include, for example, groups such as amino, carboxy or hydroxy it may be desirable to protect the group in some of the reactions mentioned herein.

A suitable protecting group for an amino or alkylamino group is, for example, an acyl group, for example an alkanoyl group such as acetyl, an alkoxycarbonyl group, for example a methoxycarbonyl, ethoxycarbonyl or *t*-butoxycarbonyl group, an arylmethoxycarbonyl group, for example benzyloxycarbonyl, or an aroyl group, for example benzoyl. The deprotection conditions for the above protecting groups necessarily vary with the choice of protecting group. Thus, for example, an acyl group such as an alkanoyl or alkoxycarbonyl group or an aroyl group may be removed for example, by hydrolysis with a suitable base such as an alkali metal hydroxide, for example lithium or sodium hydroxide. Alternatively an acyl group such as a *t*-butoxycarbonyl group may be removed, for example, by treatment with a suitable acid

as hydrochloric, sulphuric or phosphoric acid or trifluoroacetic acid and an arylmethoxycarbonyl group such as a benzyloxycarbonyl group may be removed, for example, by hydrogenation over a catalyst such as palladium-on-carbon, or by treatment with a Lewis acid for example boron tris(trifluoroacetate). A suitable alternative protecting group for a primary amino group is, for example, a phthaloyl group which may be removed by treatment with an alkylamine, for example dimethylaminopropylamine, or with hydrazine.

A suitable protecting group for a hydroxy group is, for example, an acyl group, for example an alkanoyl group such as acetyl, an aroyl group, for example benzoyl, or an arylmethyl group, for example benzyl. The deprotection conditions for the above protecting groups will necessarily vary with the choice of protecting group. Thus, for example, an acyl group such as an alkanoyl or an aroyl group may be removed, for example, by hydrolysis with a suitable base such as an alkali metal hydroxide, for example lithium or sodium hydroxide. Alternatively an arylmethyl group such as a benzyl group may be removed, for example, by hydrogenation over a catalyst such as palladium-on-carbon.

A suitable protecting group for a carboxy group is, for example, an esterifying group, for example a methyl or an ethyl group which may be removed, for example, by hydrolysis with a base such as sodium hydroxide, or for example a *t*-butyl group which may be removed, for example, by treatment with an acid, for example an organic acid such as trifluoroacetic acid, or for example a benzyl group which may be removed, for example, by hydrogenation over a catalyst such as palladium-on-carbon.

Resins may also be used as a protecting group.

The protecting groups may be removed at any convenient stage in the synthesis using conventional techniques well known in the chemical art.

A compound of the formula (I), or a pharmaceutically-acceptable salt or an *in vivo* hydrolysable ester thereof, may be prepared by any process known to be applicable to the preparation of chemically-related compounds. Such processes, when used to prepare a compound of the formula (I), or a pharmaceutically-acceptable salt or an *in vivo* hydrolysable ester thereofare provided as a further feature of the invention and are illustrated by the following representative examples. Necessary starting materials may be obtained by standard procedures of organic chemistry (see, for example, Advanced Organic Chemistry (Wiley-Interscience), Jerry March). The preparation of such starting materials is described within the accompanying non-limiting Examples. Alternatively, necessary starting materials are

obtainable by analogous procedures to those illustrated which are within the ordinary skill of an organic chemist. Information on the preparation of necessary starting materials or related compounds (which may be adapted to form necessary starting materials) may also be found in the following Patent and Application Publications, the contents of the relevant process sections of which are hereby incorporated herein by reference :

WO99/02525; WO98/54161; WO97/37980; WO97/30981 (& US5,736,545); WO97/21708 (& US5,719,154); WO97/10223; WO97/09328; WO96/35691; WO96/23788; WO96/15130; WO96/13502; WO95/25106 (& US5,668,286); WO95/14684 (& US5,652,238); WO95/07271 (& US5,688,792); WO94/13649; WO94/01110; WO93/23384 (& US5,547,950 & US 5,700,799); WO93/09103 (& US5,565,571, US5,654,428, US5,654,435, US5,756,732 & US5,801,246); US5,231,188; US5,247,090; US5,523,403; WO97/27188; WO97/30995; WO97/31917; WO98/01447; WO98/01446; WO99/10342; WO99/10343; WO99/11642; European Patent Application Nos. 0,359,418 and 0,609,905; 0,693,491 A1 (& US5,698,574); 0,694,543 A1 (& AU 24985/95); 0,694,544 A1 (& CA 2,154,024); 0,697,412 A1 (& US5,529,998); 0,738,726 A1 (& AU 50735/96); 0,785,201 A1 (& AU 10123/97); German Patent Application Nos. DE 195 14 313 A1 (& US5,529,998); DE 196 01 264 A1 (& AU 10098/97); DE 196 01 265 A1 (& AU 10097/97); DE 196 04 223 A1 (& AU 12516/97); DE 196 49 095 A1 (& AU 12517/97).

The following Patent and Application Publications may also provide useful information and the contents of the relevant process sections are hereby incorporated herein by reference :

FR 2458547; FR 2500450(& GB 2094299, GB 2141716 & US 4,476,136); DE 2923295 (& GB 2028306, GB 2054575, US4,287,351, US4,348,393, US4,413,001, US4,435,415 & US4,526,786), DE 3017499 (& GB 2053196, US4,346,102 & US4,372,967); US4,705,799; European Patent Application Nos. 0,312,000; 0,127,902; 0,184,170; 0,352,781; 0,316,594.

Information on the preparation of necessary starting materials or related compounds (which may be adapted to form necessary starting materials) may also be found in WO 01/46185.

The skilled organic chemist will be able to use and adapt the information contained and referenced within the above references to obtain necessary starting materials.

In particular we refer to our PCT patent applications WO-99/64417 and WO-00/21960 wherein detailed guidance is given on convenient methods for preparing oxazolidinone compounds.

Convenient methods include those in which as a last step;

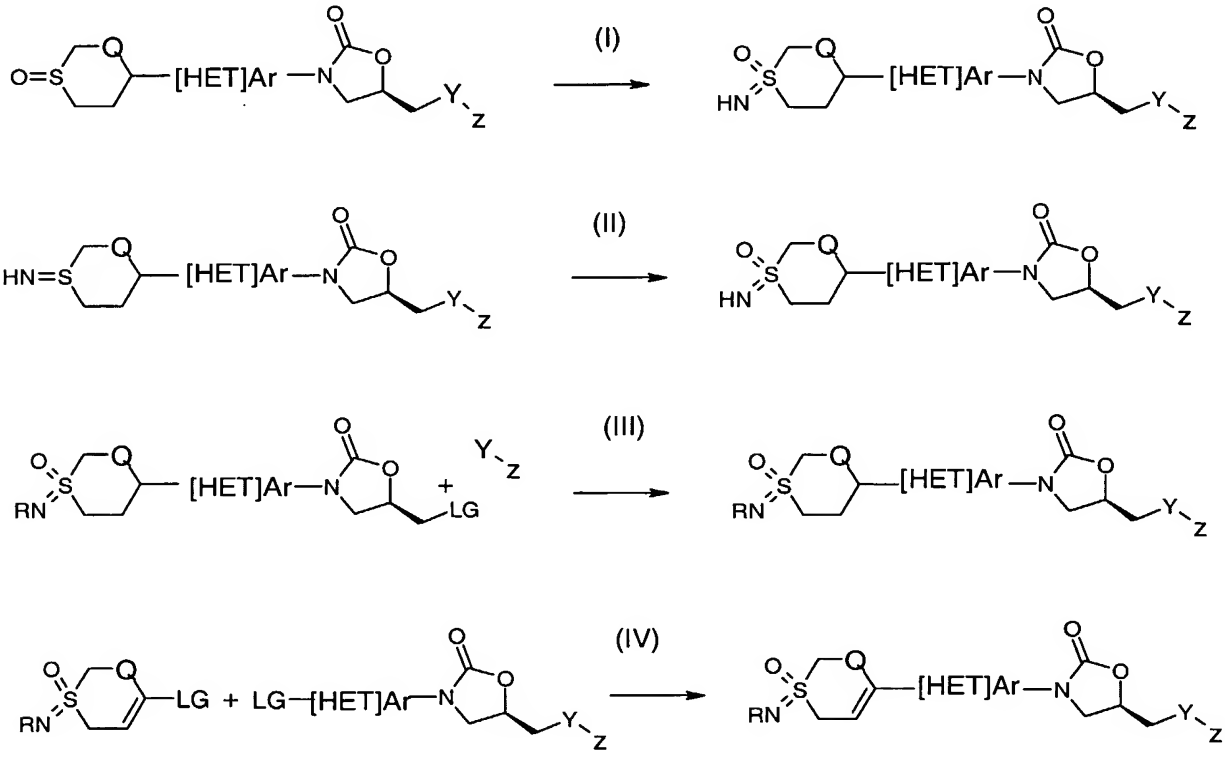
(i) a sulfoxide is converted into a sulfoximine;

(ii) a sulfilimine is oxidised to the corresponding sulfoximine

(iii) an appropriate compound heterocycle -Y-Z is coupled to an appropriate corresponding oxazolidinone intermediate.

(iv) a preformed sulfilimine or sulfoximine ring-containing intermediate is coupled to an aryloxazolidinone.

Such methods are shown by way of non-limiting illustration below wherein LG represents a convenient leaving group:

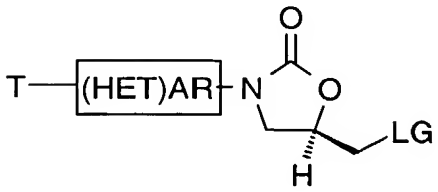


The present invention also provides that compounds of the formulae (I) and pharmaceutically-acceptable salts and *in vivo* hydrolysable esters thereof, can be prepared by a process **(a)** to **(f)** as follows (wherein the variables are as defined above unless otherwise stated) :

(a) by modifying a substituent in or introducing a substituent into another compound of

formula (I); or

(b) by reaction of a compound of formula (II) :



(II)

wherein LG is a displaceable group (which may be (i) generated in-situ, for example under Mitsunobu conditions, or (ii) preformed, such as chloro or mesylate) with a compound of the formula (III):

Y-Z

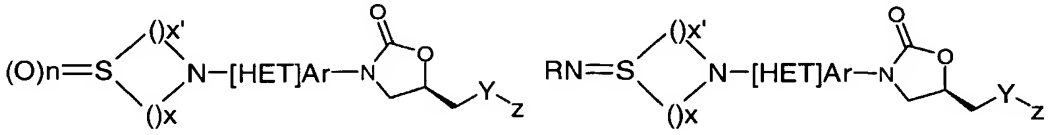
(III)

wherein heterocyclic compound Y-Z is appropriately derivatised for coupling with a compound of formula (II); or

(c) by oxidation

(i) with an aminating agent of a lower valent sulfur compound (IV), or an analogue thereof, which is suitable to give a T substituent as defined by (TA2), or a bi-, or tri-cyclic ring analogue of (IV) which is suitable to give a T substituent as defined by (TB); or

(ii) with an oxygenating agent of a lower valent sulfur compound (V), or an analogue thereof, which is suitable to give a T substituent as defined by (TA2), or a bi-, or tri-cyclic ring analogue of (V) which is suitable to give a T substituent as defined by (TB);

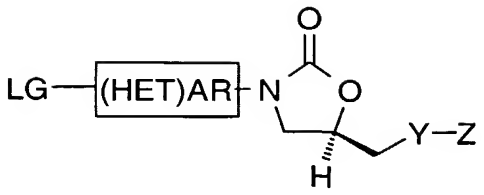


(IV) (V)

where n = 0 or 1 and ()x and ()x' are chains of length x and x'.

Suitable aminating agents include mesitylenesulfonyl hydroxylamine, sodium azide and polyphosphoric acid, and chloramine-T (T as defined by (TA2) or (TB)); suitable oxygenating agents include peracids and osmium tetroxide – amine N-oxide mixtures; or

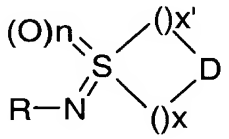
(d) (i) by coupling, using catalysis by transition metals such as palladium(0), of a compound of formula (VI) :



(VI)

wherein Y-Z is as hereinbefore defined, LG is a replaceable substituent - such as chloride, bromide, iodide, or trifluoromethylsulfonyloxy;

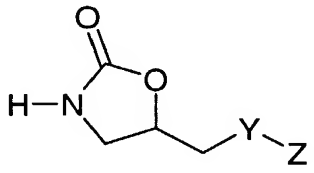
with a compound of the formula (VII), or an analogue thereof, which is suitable to give a T substituent as defined by (TA1), in which the link is via an sp^2 carbon atom, or (TA2), or a bi- or tri-cyclic ring analogue of (VII) which is suitable to give a T substituent as defined by (TB);



(VII)

where n = 0 or 1 and ()x and ()x' are chains of length x and x'; D is NH or CH=C-LG where LG is a leaving group such as chloride, bromide, iodide, or trifluoromethylsulfonyloxy; or

(d) (ii) by coupling, using catalysis by transition metals such as palladium(0), of a compound of formula (VIII):



(VIII)

wherein Y-Z is as hereinbefore defined, with a compound [Aryl]-LG, where LG is a replaceable substituent such as chloride, bromide, iodide, or trifluoromethylsulfonyloxy or an analogue thereof; or

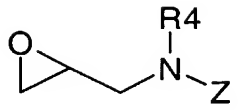
(e) by reduction of a compound formed by process (d) in which the T substituent (as defined by (TA1)) is linked via an sp^2 carbon atom, to form the saturated analogue; or

(f) by reaction of a compound of the formula (IX) :

T-Q-Z(f)

(IX)

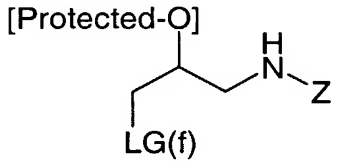
wherein Z(f) is an isocyanate, amine or urethane group with an epoxide of the formula (X):



(X)

wherein Z is an heteroaromatic group as hereinabove defined;

or with a related compound of formula (XI) where the hydroxy group at the internal C-atom is optionally conventionally protected e.g. with an acetyl group and where the leaving group LG(f) at the terminal C-atom is a conventional leaving group e.g. a chloro- or mesyloxy-group;



(XI)

General guidance on reaction conditions and reagents may be obtained in Advanced Organic Chemistry, 4th Edition, Jerry March (publisher : J.Wiley & Sons), 1992. Necessary starting materials may be obtained by standard procedures of organic chemistry, such as described in this process section, in the Examples section or by analogous procedures within the ordinary skill of an organic chemist. Certain references are also provided (see above) which describe the preparation of certain suitable starting materials, for particular example see International Patent Application Publication No. WO 97/37980, the contents of which are incorporated here by reference. Processes analogous to those described in the references may also be used by the ordinary organic chemist to obtain necessary starting materials.

a) Methods for converting substituents into other substituents are known in the art. For example an alkylthio group may be oxidised to an alkylsulfinyl or alkylsulfonyl group, a cyano group reduced to an amino group, a nitro group reduced to an amino group, a hydroxy group alkylated to a methoxy group, a hydroxy group converted to an arylthiomethyl or a heteroarylthiomethyl group (see, for example, Tet.Lett., 585, 1972), a carbonyl group converted to a thiocarbonyl group (eg. using Lawsson's reagent) or a bromo group converted to an alkylthio group. It is also possible to convert one R_{2s} group into another R_{2s} group as a final step in the preparation of a compound of the formula (I).

Convenient methods for functionalised sulfilimines and sulfoximines include those in which a sulfilimine or sulfoximine is (i) alkylated, (ii) acylated or (iii) arylated.

A detailed review of sulfoximine chemistry is provided by Michael Reggelin and Cornelia Zur in Synthesis, 2000, 1, 1-64. Further references include Reggelin et al, Tetrahedron Letters, 1992, 33 (46), 6959 - 6962; Reggelin et al, Tetrahedron Letters, 1992, 36 (33), 5885 - 5886; and Gage et al, Tetrahedron Letters, 2000, 41, 4301 - 4305.

The general method for introducing or refunctionalizing sulfimines or sulfoximines in the final step is illustrated in Scheme 1.

(b)(i) Reaction (b)(i) (in which Y is initially hydroxy) is performed under Mitsunobu conditions, for example, in the presence of tri-n-butylphosphine and diethyl azodicarboxylate (DEAD) in an organic solvent such as THF, and in the temperature range 0°C - 60°C, but preferably at ambient temperature. Details of Mitsunobu reactions are contained in Tet. Letts., 31, 699, (1990); The Mitsunobu Reaction, D.L.Hughes, Organic Reactions, 1992, Vol.42, 335-656 and Progress in the Mitsunobu Reaction, D.L.Hughes, Organic Preparations and Procedures International, 1996, Vol.28, 127-164. The general method is illustrated in Scheme 2.

(b)(ii) Reactions (b)(ii) are performed conveniently in the presence of a suitable base such as, for example, an alkali or alkaline earth metal carbonate, alkoxide or hydroxide, for example sodium carbonate or potassium carbonate, or, for example, an organic amine base such as, for example, pyridine, 2,6-lutidine, collidine, 4-dimethylaminopyridine, triethylamine, morpholine or diazabicyclo-[5.4.0]undec-7-ene, the reaction is also preferably carried out in a suitable inert solvent or diluent, for example methylene chloride, acetonitrile, tetrahydrofuran, 1,2-dimethoxyethane, *N,N*-dimethylformamide, *N,N*-dimethylacetamide, *N*-methylpyrrolidin-2-one or dimethylsulfoxide at and at a temperature in the range 25-60°C.

When Y is chloro, the compound of the formula (II) may be formed by reacting a compound of the formula (II) wherein Y is hydroxy (hydroxy compound) with a chlorinating agent. For example, by reacting the hydroxy compound with thionyl chloride, in a temperature range of ambient temperature to reflux, optionally in a chlorinated solvent such as dichloromethane or by reacting the hydroxy compound with carbon tetrachloride/triphenyl phosphine in dichloromethane, in a temperature range of 0°C to ambient temperature. A compound of the formula (II) wherein Y is chloro or iodo may also be prepared from a compound of the formula (II) wherein Y is mesylate or tosylate, by reacting the latter

compound with lithium chloride or lithium iodide and crown ether, in a suitable organic solvent such as THF, in a temperature range of ambient temperature to reflux

When Y is (1-4C)alkanesulfonyloxy or tosylate the compound (II) may be prepared by reacting the hydroxy compound with (1-4C)alkanesulfonyl chloride or tosyl chloride in the presence of a mild base such as triethylamine or pyridine.

When Y is a phosphoryl ester (such as PhO_2-P(O)-O-) or Ph_2-P(O)-O- the compound (II) may be prepared from the hydroxy compound under standard conditions.

If not commercially available, compounds of the formula (III) may be prepared by procedures which are selected from standard chemical techniques, techniques which are analogous to the synthesis of known, structurally similar compounds, or techniques which are analogous to the procedures described in the Examples. For example, standard chemical techniques are as described in Houben Weyl. The general method is illustrated in Scheme 2.

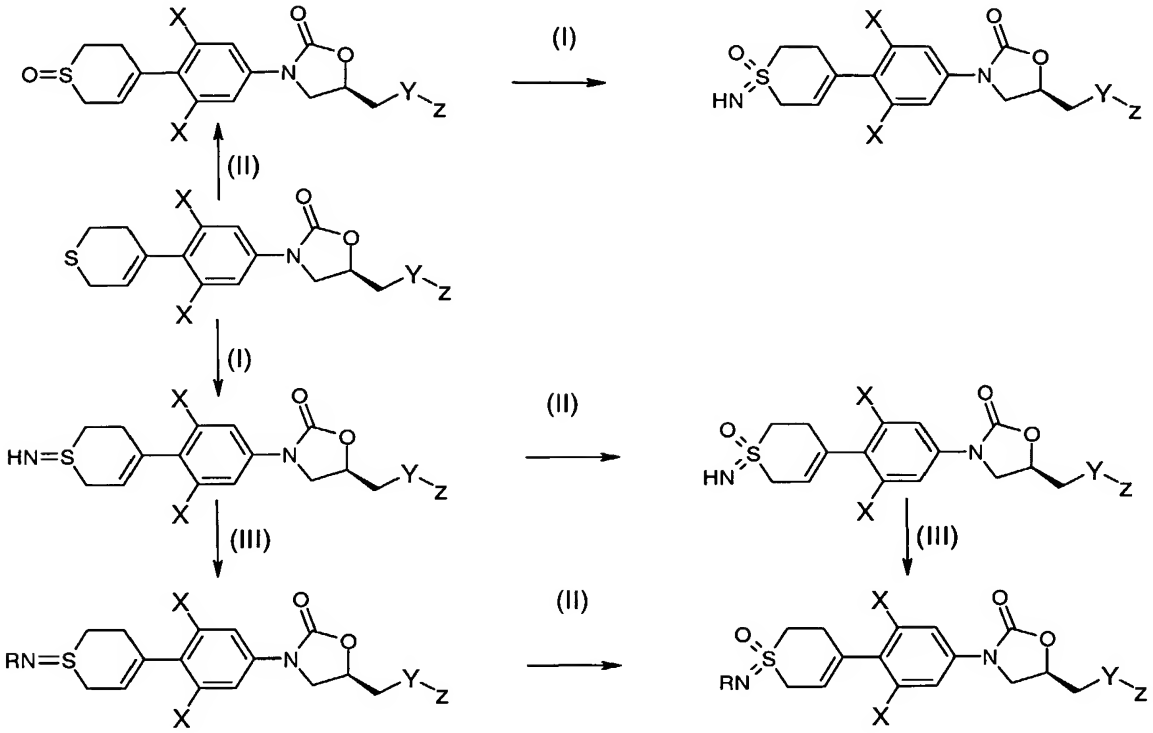
(c) Convenient methods for aminating thioethers or sulfoxides are indicated in Michael Reggelin and Cornelia Zur in Synthesis, 2000, 1, 1-64. For substrates containing nucleophilic nitrogen atoms such as tertiary arylamines it is advantageous to use an acidic reaction mixture such as sodium azide in polyphosphoric acid to reduce the amount of amination on nitrogen. Sulfoximines may be made either by oxidizing thioethers first to the corresponding sufoxides and then to the sulfoximines or by oxidizing thioethers first to the corresponding sulfilimines (sulfimines) and then to the sulfoximine. The general method for aminating thiethers or sulfoxides and for oxidizing sulfimines is illustrated in Scheme 1.

(d) The cyclic sulfoxides and sulfimines used in reaction (d) may be obtained by oxidation of the corresponding cyclic aminothioethers as illustrated in Scheme 1.

(e) The reduction of a compound formed by process (d) in which the T substituent (as defined by (TA1)) is linked via an sp^2 carbon atom, to form the saturated analogue, may be performed using standard hydrogenation. For example, a dihydrothiopyran may be reduced to produce the tetrahydrothiopyran analogue.

The following Schemes illustrate process chemistry which allows preparation of compounds of the formula (I); wherein A and R are values suitable to provide the compounds of formula (I) defined herein. The Schemes may be genericised by the skilled man to apply to compounds within the present specification which are not specifically illustrated in the

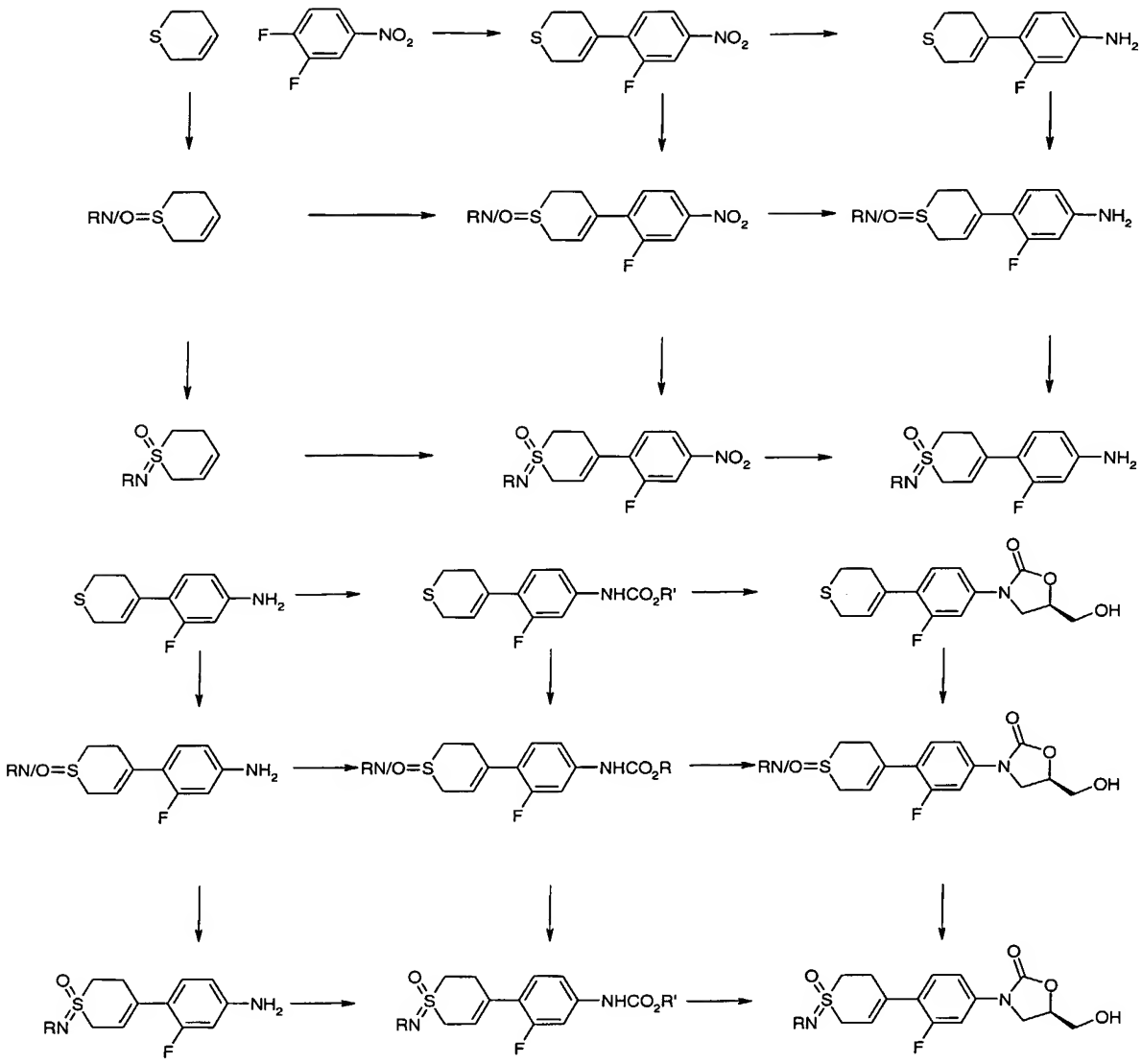
Schemes (for example to HET as a 6-membered ring as defined herein).



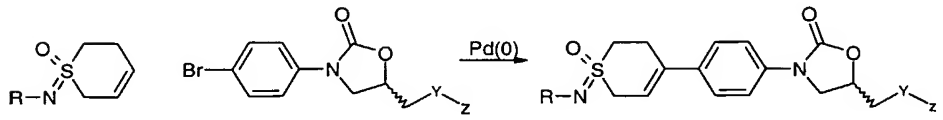
Scheme 1

(I) Amination with sodium azide/polyphosphoric acid or mesitylenesulfonylhydroxylamine;

(II) 1 equivalent m-chloroperoxybenzoic acid; (III) alkylation, arylation, or acylation according to reaction (a).



Scheme 2



Scheme 3

One compound of formula (I) may be converted into another compound of formula (I) by reacting a compound of formula (I) in which a substituent is halo with a suitable compound to form another compound. Thus, for example, halo may be displaced by suitable vinyl, aromatic, tropolone and nitrogen-linked systems by reaction using known Pd(0) coupling techniques.

Further examples of converting substituents into other substituents are contained in the accompanying non-limiting Examples.

Certain compounds may be prepared by the skilled chemist, for example as described in International Patent Application Publication Nos. WO95/07271, WO97/27188, WO 97/30995, WO 98/01446 and WO 98/01447, the contents of which are hereby incorporated by reference, and by analogous processes.

If not commercially available, compounds may be prepared by procedures which are selected from standard chemical techniques, techniques which are analogous to the synthesis of known, structurally similar compounds, or techniques which are analogous to the procedures described in the Examples. For example, standard chemical techniques are as described in Houben Weyl, Methoden der Organische Chemie, E8a, Pt.I (1993), 45-225, B.J.Wakefield (for isoxazoles) and E8c, Pt.I (1994), 409-525, U.Kraatz (for 1,2,4-oxadiazoles). Also, for example, 3-hydroxyisoxazole may be prepared by cyclisation of CH≡C-CO-NHOH (prepared from CH≡C-CO-O-(1-4C)alkyl) as described in Chem.Pharm.Bull.Japan, 14, 92, (1966).

The removal of any protecting groups, the formation of a pharmaceutically-acceptable salt and/or the formation of an *in vivo* hydrolysable ester are within the skill of an ordinary organic chemist using standard techniques. Furthermore, details on the these steps, for example the preparation of in-vivo hydrolysable ester prodrugs has been provided in the section above on such esters, and in certain of the following non-limiting Examples.

Certain novel intermediates utilised in the above processes are provided as a further feature of the invention.

When an optically active form of a compound of the formula (I) is required, it may be obtained by carrying out one of the above procedures using an optically active starting material (formed, for example, by asymmetric induction of a suitable reaction step), or by resolution of a racemic form of the compound or intermediate using a standard procedure, or

by chromatographic separation of diastereoisomers (when produced). Enzymatic techniques may also be useful for the preparation of optically active compounds and/or intermediates.

Similarly, when a pure regioisomer of a compound of the formula (I) is required, it may be obtained by carrying out one of the above procedures using a pure regioisomer as a starting material, or by separation of a mixture of the regioisomers or intermediates using a standard procedure.

According to a further feature of the invention there is provided a compound of the formula (I), or a pharmaceutically-acceptable salt, or in-vivo hydrolysable ester or amide thereof for use in a method of treatment of the human or animal body by therapy.

According to a further feature of the present invention there is provided a method for producing an antibacterial effect in a warm blooded animal, such as man, in need of such treatment, which comprises administering to said animal an effective amount of a compound of the present invention, or a pharmaceutically-acceptable salt, or in-vivo hydrolysable ester thereof.

The invention also provides a compound of the formula (I), or a pharmaceutically-acceptable salt, or in-vivo hydrolysable ester thereof, for use as a medicament, and for use as an antibacterial agent; and the use of a compound of the formula (I) of the present invention, or a pharmaceutically-acceptable salt, or in-vivo hydrolysable ester thereof, in the manufacture of a medicament for use in the production of an antibacterial effect in a warm blooded animal, such as man.

In order to use a compound of the formula (I), an in-vivo hydrolysable ester or a pharmaceutically-acceptable salt thereof, including a pharmaceutically-acceptable salt of an in-vivo hydrolysable ester, (hereinafter in this section relating to pharmaceutical composition "a compound of this invention") for the therapeutic (including prophylactic) treatment of mammals including humans, in particular in treating infection, it is normally formulated in accordance with standard pharmaceutical practice as a pharmaceutical composition.

Therefore in another aspect the present invention provides a pharmaceutical composition which comprises a compound of the formula (I), an in-vivo hydrolysable ester or a pharmaceutically-acceptable salt thereof, including a pharmaceutically-acceptable salt of an in-vivo hydrolysable ester, and a pharmaceutically-acceptable diluent or carrier.

The pharmaceutical compositions of this invention may be administered in standard manner for the disease condition that it is desired to treat, for example by oral, rectal, topical

or parenteral administration. For these purposes the compounds of this invention may be formulated by means known in the art into the form of, for example, tablets, capsules, aqueous or oily solutions or suspensions, (lipid) emulsions, dispersible powders, suppositories, ointments, creams, aerosols (or sprays), drops and sterile injectable aqueous or oily solutions or suspensions.

In addition to the compounds of the present invention the pharmaceutical composition of this invention may also contain or be co-administered (simultaneously, sequentially or separately) with one or more known drugs selected from other clinically useful antibacterial agents (for example, ß-lactams or aminoglycosides) and/or other anti-infective agents (for example, an antifungal triazole or amphotericin). These may include carbapenems, for example meropenem or imipenem, to broaden the therapeutic effectiveness. Compounds of this invention may also contain or be co-administered with bactericidal/permeability-increasing protein (BPI) products or efflux pump inhibitors to improve activity against gram negative bacteria and bacteria resistant to antimicrobial agents.

A suitable pharmaceutical composition of this invention is one suitable for oral administration in unit dosage form, for example a tablet or capsule which contains between 1mg and 1g of a compound of this invention, preferably between 100mg and 1g of a compound. Especially preferred is a tablet or capsule which contains between 50mg and 800mg of a compound of this invention, particularly in the range 100mg to 500mg.

In another aspect a pharmaceutical composition of the invention is one suitable for intravenous, subcutaneous or intramuscular injection, for example an injection which contains between 0.1% w/v and 50% w/v (between 1mg/ml and 500mg/ml) of a compound of this invention.

Each patient may receive, for example, a daily intravenous, subcutaneous or intramuscular dose of 0.5 $mgkg^{-1}$ to 20 $mgkg^{-1}$ of a compound of this invention, the composition being administered 1 to 4 times per day. In another embodiment a daily dose of 5 $mgkg^{-1}$ to 20 $mgkg^{-1}$ of a compound of this invention is administered. The intravenous, subcutaneous and intramuscular dose may be given by means of a bolus injection. Alternatively the intravenous dose may be given by continuous infusion over a period of time. Alternatively each patient may receive a daily oral dose which may be approximately equivalent to the daily parenteral dose, the composition being administered 1 to 4 times per day.

A pharmaceutical composition to be dosed intravenously may contain advantageously (for example to enhance stability) a suitable bactericide, antioxidant or reducing agent, or a suitable sequestering agent.

In the above other, pharmaceutical composition, process, method, use and medicament manufacture features, the alternative and preferred embodiments of the compounds of the invention described herein also apply.

Antibacterial Activity :

The pharmaceutically-acceptable compounds of the present invention are useful antibacterial agents having a good spectrum of activity in vitro against standard Gram-positive organisms, which are used to screen for activity against pathogenic bacteria. Notably, the pharmaceutically-acceptable compounds of the present invention show activity against enterococci, pneumococci, methicillin resistant strains of S.aureus and coagulase negative staphylococci, haemophilus and moraxella strains. The antibacterial spectrum and potency of a particular compound may be determined in a standard test system.

The (antibacterial) properties of the compounds of the invention may also be demonstrated and assessed *in-vivo* in conventional tests, for example by oral and/or intravenous dosing of a compound to a warm-blooded mammal using standard techniques.

The following results were obtained on a standard *in-vitro* test system. The activity is described in terms of the minimum inhibitory concentration (MIC) determined by the broth-dilution technique with an inoculum size of $5x10^4$ CFU/spot. Typically, compounds are active in the range 0.01 to 256 μg/ml.

Staphylococci were tested in broth using an inoculum of $5x10^4$ CFU/spot and an incubation temperature of 37°C for 16-24hours.

Streptococci were tested in Mueller-Hinton broth supplemented with 2.5% clarified lake horse blood with an innoculum of 10^4 CFU/well and an incubation temperature of 37°C aerobically for 24 hours.

Fastidious Gram negative organisms were tested in Mueller-Hinton broth supplemented with hemin and NAD, grown aerobically for 24h at 37°C, and with an innoculum of $5x10^4$ CFU/well.

Organism		MIC (μg/ml) Example 4
Staphylococcus aureus:		
	MSQS	1
	MRQR	4
Streptococcus pneumoniae		0.5
Streptococcus pyogenes		1
Haemophilus influenzae		2
Moraxella catarrhalis		8

MSQS = methicillin sensitive and quinolone sensitive

MRQR = methicillin resistant and quinolone resistant

The invention is now illustrated but not limited by the following Examples in which unless otherwise stated :-

i) evaporations were carried out by rotary evaporation in vacuo and work-up procedures were carried out after removal of residual solids by filtration;

(ii) operations were carried out at ambient temperature, that is typically in the range 18-26°C and in air unless otherwise stated, or unless the skilled person would otherwise work under an inert atmosphere;

(iii) column chromatography (by the flash procedure) was used to purify compounds and was performed on Merck Kieselgel silica (Art. 9385) unless otherwise stated;

(iv) yields are given for illustration only and are not necessarily the maximum attainable;

(v) the structure of the end-products of the formula (I) were generally confirmed by NMR and mass spectral techniques [proton magnetic resonance spectra were generally determined in DMSO-D6 unless otherwise stated using a Varian Gemini 2000 spectrometer operating at a field strength of 300 MHz, or a Bruker AM250 spectrometer operating at a field strength of 250 MHz; chemical shifts are reported in parts per million downfield from tetramethysilane as an internal standard (δ scale) and peak multiplicities are shown thus: s, singlet; d, doublet; AB or dd, doublet of doublets; t, triplet, m, multiplet; fast-atom bombardment (FAB) mass spectral data were generally obtained using a Platform spectrometer (supplied by Micromass)

run in electrospray and, where appropriate, either positive ion data or negative ion data were collected];

(vi) intermediates were not generally fully characterised and purity was in general assessed by thin layer chromatographic, infra-red (IR), mass spectral (MS) or NMR analysis; and

(vii) in which the following abbreviations may be used :-

® is a Trademark; DMF is N,N-dimethylformamide; DMA is N,N-dimethylacetamide;TLC is thin layer chromatography; HPLC is high pressure liquid chromatography; MPLC is medium pressure liquid chromatography; DMSO is dimethylsulfoxide; DMSO-d6 is deuterated DMSO; $CDCl_3$ is deuterated chloroform; MS is mass spectroscopy; ESP is electrospray; THF is tetrahydrofuran; TFA is trifluoroacetic acid; NMP is N-methylpyrrolidone; HOBT is 1-hydroxy-benzotriazole; EtOAc is ethyl acetate; MeOH is methanol; phosphoryl is $(HO)_2$-P(O)-O-; phosphiryl is $(HO)_2$-P-O-; EDC is 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (hydrochloride); PTSA is para- toluenesulfonic acid.

It is to be understood that the compounds:

cis and *trans*-(*5S*)-{3-[3-Fluoro-4-(1-imino-1-oxo-tetrahydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-ylaminomethyl)-oxazolidin-2-one;

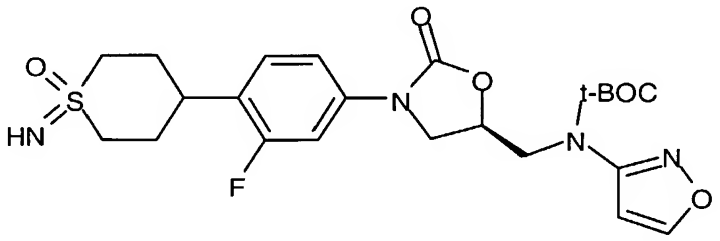
Acetic acid *cis* and *trans*-(*5S*)-(4-{2-fluoro-4-[5-(isoxazol-3-ylaminomethyl)-2-oxo-oxazolidin-3-yl]-phenyl}-1-oxo-tetrahydrothiopyran-1-ylidenecarbamoyl)-methyl ester; and

Cis and *trans*-(*5S*)-*N*-(4-{2-fluoro-4-[5-(isoxazol-3-ylaminomethyl)-2-oxo-oxazolidin-3-yl]-phenyl}-1-oxo-tetrahydrothiopyran-1-ylidene)-2-hydroxy-acetamide;

referred to in examples 3, 5 and 6 respectively, do not form part of the present invention.

Examples

Example 1: *cis* and *trans*-(5*R*)-{3-[3-Fluoro-4-(1-imino-1-oxo-tetrahydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester



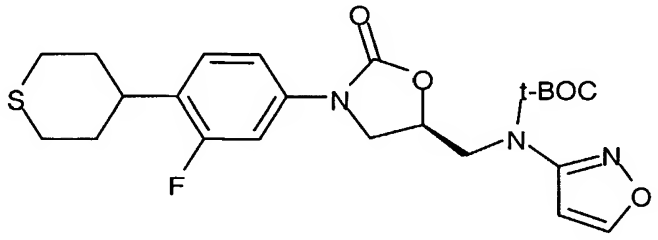
(5*R*)-{3-[3-fluoro-4-(1-oxo-tetrahydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester (mix of cis and trans isomers,800 mg, 1.62 mM) was dissolved in dichloromethane (6.5 ml) at ambient temperature. *O*-Mesitylene-sulfonylhydroxylamine (383 mg, 1.77 mM, see Synthesis, 1972, 140), in dichloromethane (6.5 ml) was added dropwise, and the mixture stirred at ambient temperature for 18 hours. The resulting precipitate was filtered, washed with a little dichloromethane, and dried to give the title compound (236 mg) as its mesitylene sulfonate salt.

MS (ESP): 509 (MH^+) for $C_{23}H_{29}FN_4O_6S$

NMR (DMSO-d_6) δ: 1.49 (s, 9H); 2.16 (s, 3H); 2.20 (br m, 4H); 2.50 (overlapped by DMSO, ~6H); 3.37 (br m, 1H); 3.84 (dd, 1H); 4.00 (br m, 4H); 4.20 (t, 1H); 4.25 (m, 2H); 5.00 (m, 1H); 6.74 (s, 2H); 6.87 (d, 1H); 7.34 (t, 1H); 7.37 (dd, 1H); 7.49 (dd, 1H); 8.81 (d, 1H); 2 exchangeables not seen; complex spectrum resulting from mix of *cis* and *trans* isomers.

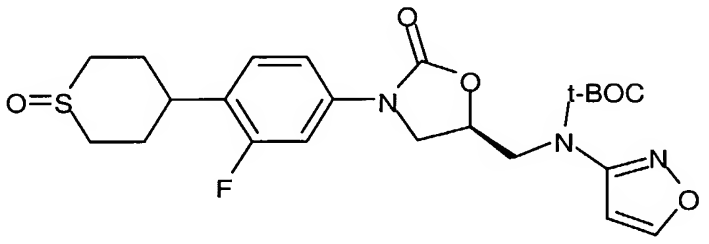
The intermediates for this compound were prepared as follows:

(*5R*)-{3-[3-Fluoro-4-(tetrahydro-thiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester



Sodium hydride (50% in oil, 264 mg, 5.5 mM) was suspended in dry *N*,*N*-dimethylformamide (10 ml) under nitrogen, and 3-*tert*-butoxycarbonylaminoisoxazole (1.01 g, 5.5 mM) added. After warming for 15 minutes at 35°, methanesulfonic acid (*5R*)-3-[3-fluoro-4-(tetrahydro-thiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl ester (1.95 g, 5 mM) was added, and the mixture heated to 50° for 1.5 hours. After cooling, the mixture was diluted with aqueous sodium bicarbonate (5%, 200 ml), and extracted with ethyl acetate (2 x 150 ml). The organic phase was washed with water (2 x 150 ml) and brine (100 ml), dried (magnesium sulfate) and evaporated to give product (2.5 g) sufficiently pure for further chemistry. The crude product was used directly in the next step.

Cis and *trans*-(*5R*)-{3-[3-Fluoro-4-(1-oxo-tetrahydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester



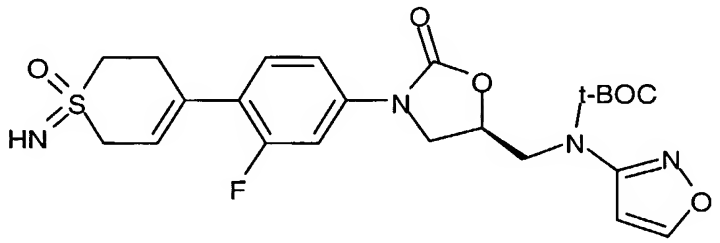
Crude {3-[3-fluoro-4-(tetrahydro-thiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester (1.17 g, 2.45 mM) from above was stirred in a mixture of methanol (18.3ml) and ethyl acetate (12.2 ml) at ambient temperature. Sodium periodate (918 mg, 4.28 mM) in water (12.2 ml) was added dropwise, and the mixture stirred for 18 hours. Brine (200 ml) was added, and the mixture extracted with ethyl acetate

(200 ml). The organic phase was separated, washed with brine (100 ml), dried (magnesium sulfate), filtered and evaporated. Crude product was chromatographed on a 20 g silica Mega Bond Elut® column, eluting with a gradient from 0 to 100% ethyl acetate in dichloromethane, then 0 to 10% methanol in dichloromethane. Relevant fractions were combined to give the desired product (800 mg).

MS (ESP): 494 (MH^+) for $C_{23}H_{28}FN_3O_6S$

NMR (DMSO-d_6) δ: 1.48 (s, 9H); 1.68 (d, ~2H); 1.94 (m, ~1H); 2.33 (dd, 2H); 2.82 (tm, 2H); 2.95 (d, 1H); 3.05 (t, 1H); 3.84 (dd, 1H); 3.98 (dd, 1H); 4.23 (m, 2H); 4.99 (m, 1H); 6.87 (d, 1H); 7.23-7.48 (overlapping m, 3H); 8.80 (d, 1H); complex spectrum resulting from mix of *cis* and *trans* isomers.

Example 2: (*5R*)-{3-[3-Fluoro-4-(*1RS*-1-imino-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester

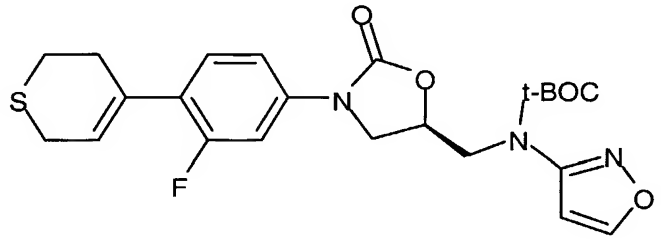


Using essentially the procedure Example 1 but starting from (*5R*)-{3-[3-fluoro-4-(1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester (500 mg, 1.02 mM) gave the title compound (183 mg) as its mesitylene sulfonate salt.

NMR (DMSO-d_6) δ: 1.49 (s, 9H); 2.16 (s, 3H); 2.49 (overlapped by DMSO, ~6H); 3.05 (br m, 2H); 3.87 (dd, 1H); 4.02 (overlapping m, 3H); 4.23 (t overlapping m, 2H); 4.54 (m, 2H); 5.01 (m, 1H); 5.91 (t, 1H); 6.73 (s, 2H); 6.86 (d, 1H); 7.38 (m, 2H); 7.52 (dd, 1H); 8.81 (d, 1H); 2 exchangeables not seen.

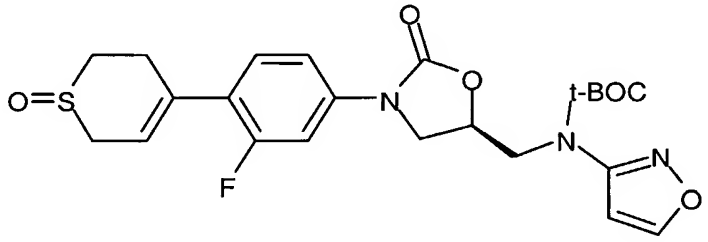
The intermediates for this compound were prepared as follows

(*5R*)-{3-[4-(3,6-Dihydro-2*H*-thiopyran-4-yl)-3-fluoro-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester



Using essentially the procedure of appropriate intermediate of Example 1, but starting from methanesulfonic acid (*5R*)-3-[4-(3,6-dihydro-2*H*-thiopyran-4-yl)-3-fluoro-phenyl]-2-oxo-oxazolidin-5-ylmethyl ester (1.95 g, 5 mM) gave product (2.2 g) sufficiently pure for further chemistry.

(*5R*)-{3-[3-Fluoro-4-(*1RS*-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester

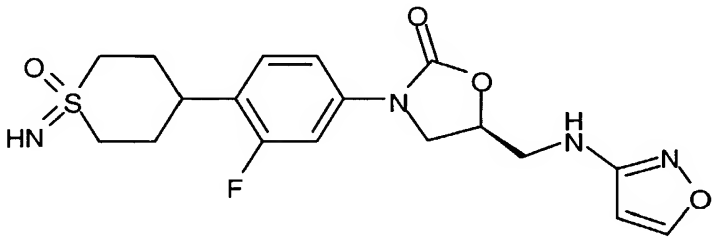


Essentially the procedure of the relevant intermediate of Example 1 was used, but starting from (*5R*)-{3-[4-(3,6-dihydro-2*H*-thiopyran-4-yl)-3-fluoro-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester (1.19 g, 2.5 mM). Crude product was chromatographed on a 20 g silica Mega Bond Elut® column, eluting with a gradient from 0 to 100% ethyl acetate in dichloromethane, then 0 to 10% methanol in dichloromethane. Relevant fractions were combined to give the desired product (500 mg).

MS (ESP): 492 (MH^+) for $C_{23}H_{26}FN_3O_6S$

NMR (DMSO-d_6) δ: 1.49 (s, 9H); 2.59 (t, 1H); 2.81 (overlapping m, 2H); 3.11 (m, 1H); 3.37 (dd, 1H); 3.66 (d, 1H); 3.88 (dd, 1H); 3.98 (dd, 1H); 4.25 (overlapping m, 2H); 5.00 (m, 1H); 5.81 (br, 1H); 6.87 (d, 1H); 7.34 (dd, 1H); 7.41 (t, 1H); 7.50 (dd, 1H); 8.82 (d, 1H).

Example 3: *cis* and *trans*-(*5S*)-{3-[3-Fluoro-4-(1-imino-1-oxo-tetrahydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-ylaminomethyl)-oxazolidin-2-one



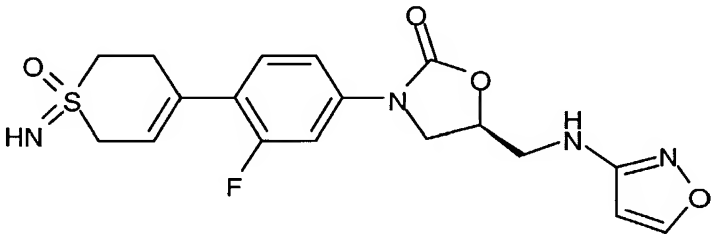
(*5R*)-3-[3-Fluoro-4-(1-imino-1-oxo-tetrahydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester mesitylene sulfonate salt (150 mg, 0.21 mM) was stirred at ambient temperature in dichloromethane (5 ml), and trifluoroacetic acid (5 ml) added.

After stirring 1 hour, solvent was evaporated, the residue dissolved in the minimum of dichloromethane and the desired product precipitated by the addition of diethyl ether, as its mesitylene sulfonate salt (126 mg).

MS (ESP): 409 (MH^+) for $C_{18}H_{21}FN_4O_4S$

NMR (DMSO-d_6) δ: 2.16 (s, 3H); 2.21 (m, 4H); 2.51 (overlapped by DMSO, ~6H); 3.43 (m, 3H); 3.81 (dd, 1H); 4.01 (overlapping m, 4H); 4.16 (t, 1H); 4.88 (m, 1H); 6.01 (d, 1H); 6.52 (br, 1H); 6.74 (s, 2H); 7.30 (dd, 1H); 7.35 (t, 1H); 7.50 (dd, 1H); 8.38 (d, 1H); 2 exchangeables not seen; complex spectrum resulting from mix of *cis* and *trans* isomers.

Example 4: (*5S*)-3-[3-Fluoro-4-(*1RS*-1-imino-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-ylaminomethyl)-oxazolidin-2-one



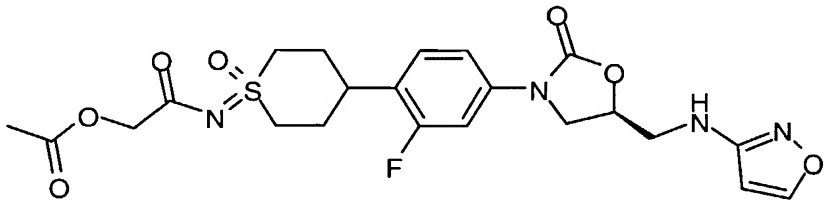
Using essentially the procedure of Example 3, but starting from (*5R*)-{3-[3-fluoro-4-((*1RS*)-1-imino-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester mesitylene sulfonate salt (105 mg, 0.15 mM)

gave the title compound (96 mg) as its mesitylene sulfonate salt.

NMR (DMSO-d_6) δ: 2.16 (s, 3H); 2.49 (overlapped by DMSO, ~6H); 3.04 (br m, 2H); 3.44

(m, 2H); 3.83 (dd, 1H); 4.01 (m, 1H); 4.08 (dd, 1H); 4.17 (t, 1H); 4.55 (m, 2H); 4.90 (m, 1H); 5.89 (t, 1H); 5.99 (d, 1H); 6.52 (br, 1H); 6.73 (s, 2H); 7.35 (dd, 2H); 7.40 (t, 1H); 7.56 (dd, 1H); 8.39 (d, 1H); 2 exchangeables not seen.

Example 5: Acetic acid *cis* and *trans*-(5*S*)-(4-{2-fluoro-4-[5-(isoxazol-3-ylaminomethyl)-2-oxo-oxazolidin-3-yl]-phenyl}-1-oxo-tetrahydrothiopyran-1-ylidenecarbamoyl)-methyl ester



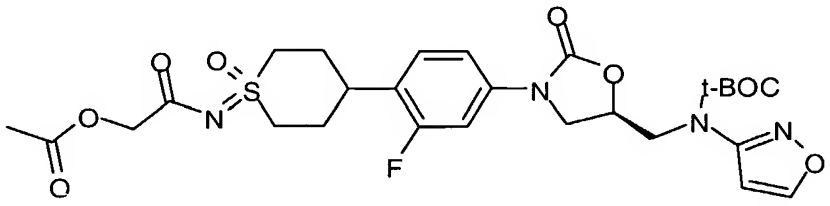
Using essentially the procedure of Example 3, but starting from acetic acid (*5R*)-[4-(4-{5-[(*tert*-butoxycarbonyl-isoxazol-3-yl-amino)-methyl]-2-oxo-oxazolidin-3-yl}-2-fluoro-phenyl)-1-oxo-tetrahydrothiopyran-1-ylidenecarbamoyl]-methyl ester (268 mg, 0.53 mM) gave the title compound (236 mg) as a precipitate from methanol / dichloromethane.

MS (ESP): 509 (MH^+) for $C_{22}H_{25}FN_4O_7S$

NMR ($CDCl_3$) δ: 2.09 (s, 3H); 2.14 (m, 2H); 2.23 (m, 2H); 3.27 (m overlapping H_2O, 1H); 3.45 (t, 2H); 3.59 (td, 2H); 3.71 (m, 2H); 3.81 (dd, 1H); 4.15 (t, 1H); 4.50 (s, 2H); 4.87 (m, 1H); 6.00 (d, 1H); 6.53 (t, 1H); 7.28 (dd, 1H); 7.39 (t, 1H); 7.49 (dd, 1H); 8.38 (d, 1H).

The intermediate for this compound was prepared as follows

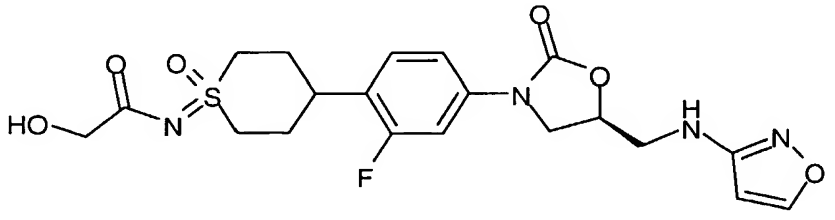
Acetic acid *cis* and *trans*-(5*R*)*N*-[4-(4-{5-[(*tert*-butoxycarbonyl-isoxazol-3-yl-amino)-methyl]-2-oxo-oxazolidin-3-yl}-2-fluoro-phenyl)-1-oxo-tetrahydrothiopyran-1-ylidenecarbamoyl]-methyl ester



(5*R*)-3-[3-fluoro-4-(1-imino-1-oxo-tetrahydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester mesitylene sulfonate salt (370 mg, 0.52 mM) was stirred in a mixture of acetoxyacetyl chloride(4ml) and saturated aqueous sodium bicarbonate (6 ml) at ambient temperature, and acetic anhydride (0.5 ml, excess) was added dropwise. After stirring 2 hours, ethyl acetate was added, the organic layer was separated, washed with sodium bicarbonate water, dried (magnesium sulfate) and evaporated. The residue was purified by chromatography on a 10 g silica Mega Bond Elut® column, and eluted with a gradient increasing in polarity from 0 to 100% ethyl acetate in dichloromethane, then 0 to 10% methanol in dichloromethane. Relevant fractions were combined to give the title compound (269 mg)..

MS (ESP): 609 (MH^+) for $C_{27}H_{33}FN_4O_9S$

Example 6: *Cis* and *trans*-(5*S*)-*N*-(4-{2-fluoro-4-[5-(isoxazol-3-ylaminomethyl)-2-oxo-oxazolidin-3-yl]-phenyl}-1-oxo-tetrahydrothiopyran-1-ylidene)-2-hydroxy-acetamide

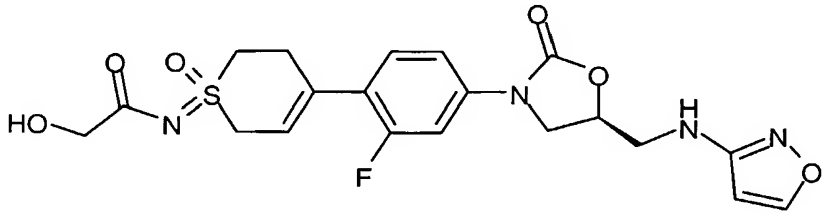


Using essentially the procedure of Example 15 , but starting from acetic acid (5*S*)-(4-{2-fluoro-4-[5-(isoxazol-3-ylaminomethyl)-2-oxo-oxazolidin-3-yl]-phenyl}-1-oxo-tetrahydrothiopyran-1-ylidenecarbamoyl)-methyl ester (130 mg, 0.25 mM) gave the title

compound (37 mg) after chromatography.

MS (ESP): 467 (MH^+) for $C_{20}H_{23}FN_4O_6S$

Example 7: (*5S*)-*N*-(4-{2-Fluoro-4-[5-(isoxazol-3-yloxymethyl)-2-oxo-oxazolidin-3-yl]-phenyl}-*1RS*-1-oxo-,3,6-dihydrothiopyran-1-ylidene)-2-hydroxy-acetamide



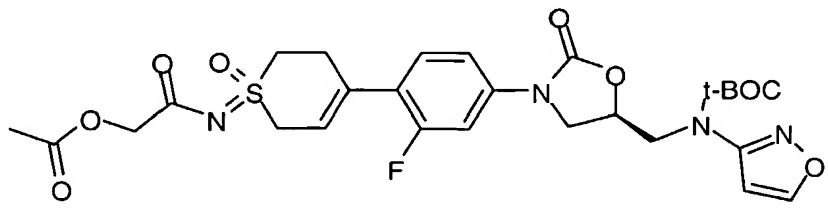
Using essentially the procedure of Example 15 , but starting from acetic acid (*5S*)-(4-{2-fluoro-4-[5-(isoxazol-3-ylaminomethyl)-2-oxo-oxazolidin-3-yl]-phenyl}-*1RS*-1-oxo-3,6-dihydrothiopyran-1-ylidenecarbamoyl)-methyl ester (50 mg, 0.11 mM) gave the title compound (19 mg) after chromatography.

MS (Negative ESP): 463 ($M-H^-$) for $C_{20}H_{21}FN_4O_6S$

NMR (DMSO-d_6) δ: 2.94 (br, 2H); 3.43 (t, 2H); 3.72 (t, 2H); 3.80 (dd, 1H); 3.90 (d, 2H); 4.17 (t, 1H); 4.26 (dd, 1H); 4.42 (dd, 1H); 4.75 (t, 1H); 4.88 (m, 1H); 5.85 (t, 1H); 5.99 (d, 1H); 6.41 (t, 1H); 7.33 (dd, 1H); 7.40 (t, 1H); 7.51 (dd, 1H); 8.38 (d, 1H).

The intermediates for this compound were prepared as follows

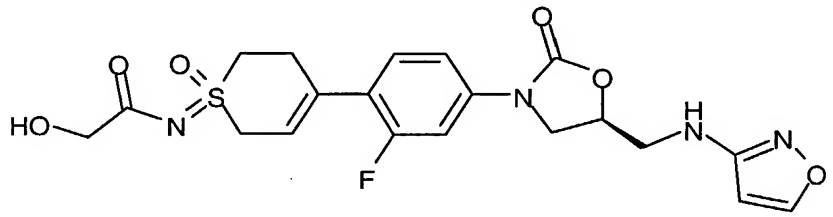
Acetic acid (*5R*)-[4-(4-{5-[(*tert*-butoxycarbonyl-isoxazol-3-yl-amino)-methyl]-2-oxo-oxazolidin-3-yl}-2-fluoro-phenyl)-*1RS*-1-oxo-3,6-dihydrothiopyran-1-ylidenecarbamoyl]-methyl ester



Using essentially the procedure for the intermediate for Example 7, but starting from (*5R*)-{3-[3-fluoro-4-(*1RS*-1-imino-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester mesitylene sulfonate salt (210 mg, 0.30 mM) and acetoxyacetyl chloride gave the title compound (68 mg) after chromatography.

MS (ESP): 607 (MH^+) for $C_{27}H_{31}FN_4O_9S$

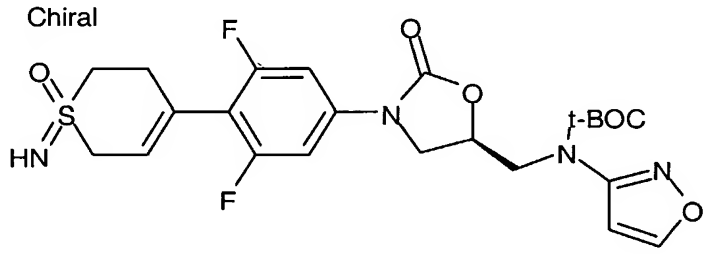
Acetic acid (*5S*)-(4-{2-fluoro-4-[5-(isoxazol-3-ylaminomethyl)-2-oxo-oxazolidin-3-yl]-phenyl}-*1RS*-1-oxo-3,6-dihydrothiopyran-1-ylidenecarbamoyl)-methyl ester



Using essentially the procedure of Example 3, but starting from acetic acid (*5R*)-[4-(4-{5-[(*tert*-butoxycarbonyl-isoxazol-3-yl-amino)-methyl]-2-oxo-oxazolidin-3-yl}-2-fluoro-phenyl)-*1RS*-1-oxo-3,6-dihydrothiopyran-1-ylidenecarbamoyl]-methyl ester (67 mg, 0.13 mM) gave the title product (50 mg).

MS (ESP): 507 (MH^+) for $C_{22}H_{23}FN_4O_7S$

Example 8: (*5R*)-{3-[3,5-Difluoro-4-(*1RS*-1-imino-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester



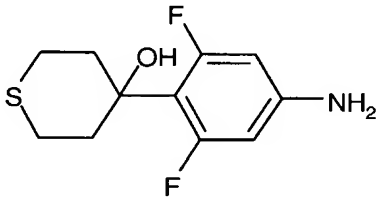
Using essentially the procedure for Example 1 but starting from (*5R*)-{3-[3,5-difluoro-4-(*1RS*-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester (4.4 g, 8.64 mM), gave the title product (3.4 g) as its mesitylenesulfonate salt.

MS (ESP): 525 (MH^+) for $C_{23}H_{26}F_2N_4O_6S$

NMR (DMSO-d_6) δ: 1.48 (s, 9H); 2.16 (s, 3H); 2.48 (overlapped by DMSO, ~6H); 2.94 (br m, 2H); 3.87 (dd, 1H); 3.98 (dd overlapping m, 2H); 4.10 (t, 1H); 4.15-4.32 (overlapping m, 2H); 4.60 (br, 2H); 5.03 (m, 1H); 5.86 (br, 1H); 6.73 (s, 2H); 6.85 (d, 1H); 7.39 (d, 2H); 8.81 (d, 1H); 2 exchangeables not seen.

The intermediates for this compound were prepared as follows

4-Hydroxy-4-(2,6-difluoro-4-aminophenyl)tetrahydrothiopyran

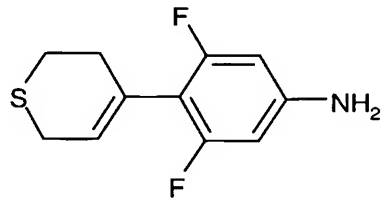


3,5-Difluoroaniline (12.9 g, 0.1 M) was reacted with tetrahydrothiopyran-4-one under essentially the following conditions (except that *n*-butyllithium was used to generate both anions): dissolved in dry tetrahydrofuran (400 ml), stirred under nitrogen, and cooled to -78°. *n*-Butyllithium (1.6M in hexanes, 131 ml, 0.21 M) was run in over 15 minutes, keeping the temperature below -65°, and the mixture then stirred a further 30 minutes at -70°. Chlorotrimethylsilane (22.8 g, 0.21 M) in tetrahydrofuran (100 ml) was added dropwise over 15 minutes, keeping the temperature below -65°, after which the temperature was allowed to rise to ambient, and stirring continued for 40 minutes to complete the silylation. The mixture was then recooled to -78°, and *sec*-butyllithium (1.3M in cyclohexane, 84.3 ml, 0.11 M) added dropwise, and stirring continued at this temperature for 5 hours. A solution of tetrahydrothiopyran-4-one (12.5 g, 0.107 M) in tetrahydrofuran (80 ml) was added dropwise below -70°, and the temperature of the mixture allowed to come to ambient over 18 hours. After cooling in an ice-bath, the reaction was acidified with 1M hydrochloric acid to a pH <1 (~500 ml), stirred 15 minutes, diethyl ether (1 L) added, and the phases separated. The organic layer was washed with 1M hydrochloric acid (200 ml), the combined aqueous layers washed with diethyl ether (200 ml), then made basic with 880 ammonia plus a little ice, then re-extracted with diethyl ether (600 ml). The organic extract was washed with brine (300 ml), dried (magnesium sulfate), filtered and evaporated. Crude product was dissolved in hot dichloromethane (400 ml), evaporated to a low volume, then diluted with *iso*hexane (300 ml). The desired product was precipitated from dichloromethane by *iso*hexane to give a white solid (17.4 g).

MS (Negative ESP): 244 ($M-H^-$) for $C_{11}H_{13}F_2NOS$

NMR ($CDCl_3$) δ: 2.26 (d, 2H); 2.39 (t, 4H); 2.65 (t, 1H); 3.27 (t, 2H); 3.82 (br, 2H); 6.17 (d, 2H).

4-(2,6-Difluoro-4-aminophenyl)-3,6-dihydro-2*H*-thiopyran

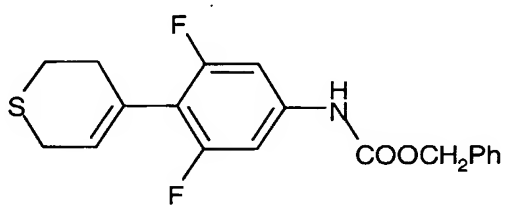


4-Hydroxy-4-(2,6-difluoro-4-aminophenyl)tetrahydrothiopyran (16.7 g, 68 mM) was treated with concentrated hydrochloric acid under essentially the following conditions: butylated hydroxytoluene (50 mg) used as antioxidant, materials were suspended in a mixture of concentrated hydrochloric acid (37%, 200 ml) and water (50 ml), and stirred at 80° under nitrogen for 18 hours. Glacial acetic acid (150 ml) was added, and reaction continued at 80° for a further 5 hours. After cooling, the reaction was made basic by the cautious addition of concentrated ammonia and ice. The mixture was extracted with diethyl ether (400 ml), the extract washed with water (100 ml), brine (100 ml), dried (magnesium sulfate), filtered and evaporated to give the title product (15.2 g) as a cream solid.

MS (ESP): 228 (MH^+) for $C_{11}H_{11}F_2NS$

NMR ($CDCl_3$) δ: 2.48 (m, 2H); 2.83 (t, 2H); 3.30 (m, 2H); 3.80 (br, 2H); 5.87 (m, 1H); 6.16 (d, 2H).

4-(2,6-Difluoro-4-benzyloxycarbonylaminophenyl)-3,6-dihydro-2*H*-thiopyran



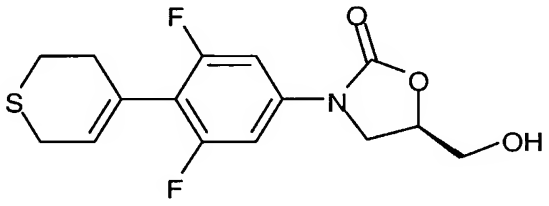
4-(2,6-Difluoro-4-aminophenyl)-3,6-dihydro-2*H*-thiopyran (15 g, 66 mM) was treated with benzyl chloroformate under essentially the following conditions: material was dissolved in dry dichloromethane (175 ml), pyridine (5.57 g, 70.6 mM) added, and the mixture stirred under nitrogen at -20°. A solution of benzyl chloroformate (8.52 g, 49.9 mM) dissolved in dry dichloromethane (20 ml) was added dropwise, and the mixture left to warm to ambient temperature over 18 hours. The mixture was washed with 1M hydrochloric acid (200 ml), then brine (100 ml), dried (magnesium sulfate), filtered and evaporated to a small volume.

The addition of *iso*hexane (300 ml) precipitated the desired product. Similar treatment of the mother liquors from filtration gave more material; total yield (22.5 g).

MS (Negative ESP): 360 ($M-H^-$) for $C_{19}H_{17}F_2NO_2S$

NMR (DMSO-d_6) δ: 2.37 (br, 2H); 2.78 (t, 2H); 3.24 (m, 2H); 5.16 (s, 2H); 5.89 (m, 1H); 7.17 (d, 2H); 7.38 (m, 5H); 10.18 (s, 1H).

(5*R*)-3-(4-(3,6-Dihydro-2*H*-thiopyran-4-yl)-3,5-difluorophenyl)-5-hydroxymethyloxazolidin-2-one



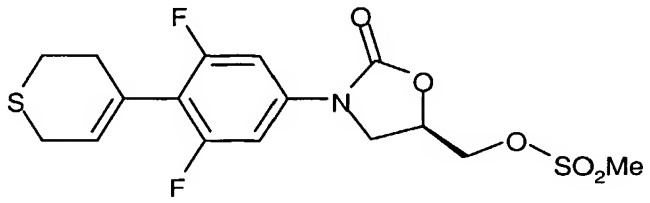
4-(2,6-Difluoro-4-benzyloxycarbonylaminophenyl)-3,6-dihydro-2*H*-thiopyran (22 g, 61 mM) was reacted with (*R*)-glycidyl butyrate under essentially the following conditions: material was dissolved in dry tetrahydrofuran (150 ml), and stirred under nitrogen at -70°. *n*-Butyllithium (1.6M in hexanes, 26 ml, 41.6 mM) was run in over 20 minutes, keeping the temperature below -60°, and the mixture then stirred a further 10 minutes at -70°. A solution of (*R*)-glycidyl butyrate (5.59 g, 38.8 mM) dissolved in dry tetrahydrofuran (10 ml) was added dropwise over 10 minutes keeping temperature below -60°, and the mixture left to warm to ambient temperature over 18 hours. Methanol (25 ml) was added, and the mixture stirred for 10 minutes only.

Saturated aqueous sodium bicarbonate (200 ml) was added, and the mixture extracted with ethyl acetate (400 ml). The extract was washed with saturated aqueous sodium bicarbonate (100 ml), brine (100 ml), dried (magnesium sulfate), filtered and evaporated. Crude product from the final extraction was precipitated from dichloromethane by *iso*hexane, then recrystallised from isopropanol to give the desired product (16.2 g).

MS (ESP): 328 (MH^+) for $C_{15}H_{15}F_2NO_3S$

NMR (DMSO-d_6) δ: 2.40 (m, 2H); 2.81 (t, 2H); 3.28 (m, 2H); 3.53 (m, 1H); 3.67 (m, 1H); 3.82 (dd, 1H); 4.08 (t, 1H); 4.70 (m, 1H); 5.21 (t, 1H); 5.95 (s, 1H); 7.33 (d, 2H).

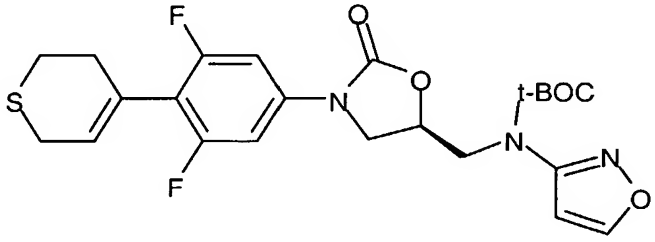
Methanesulfonic acid (*5R*)-3-[4-(3,6-dihydro-2*H*-thiopyran-4-yl)-3,5-difluoro-phenyl]-2-oxo-oxazolidin-5-ylmethyl ester



(*5R*)-3-(4-(3,6-dihydro-2*H*-thiopyran-4-yl)-3,5-difluorophenyl)-5-hydroxymethyloxazolidin-2-one (3.27 g, 10 mM) was stirred in dichloromethane (100 ml) under nitrogen, and cooled in an ice-bath. Triethylamine (1.43g, 14 mM) was added, followed by dropwise addition of methanesulfonyl chloride (1.37g, 12mM), and the mixture stirred at 0-5° for 2 hours. Saturated aqueous sodium bicarbonate (100 ml) was added, the organic phase separated, washed with 1M hydrochloric acid (50 ml), then aqueous sodium bicarbonate (50 ml), dried (magnesium sulfate), filtered and evaporated. The residue was slurried in dichloromethane (50 ml), diluted with *iso*hexane (200 ml) to give a precipitate of the title product (4.2 g) of sufficient purity for further chemistry.

MS (Negative ESP): 450 ($M-H^-$) for $C_{16}H_{17}F_2NO_5S_2$ + HCOOH

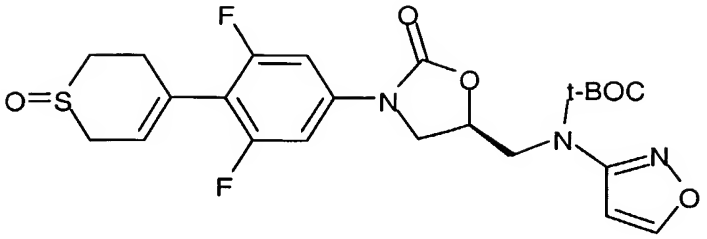
(*5R*)-{3-[4-(3,6-Dihydro-2*H*-thiopyran-4-yl)-3,5-difluoro-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester



Using essentially the procedure of the appropriate intermediate of Example 1, but starting from methanesulfonic acid (*5R*)-3-[4-(3,6-dihydro-2*H*-thiopyran-4-yl)-3,5-difluoro-phenyl]-2-oxo-oxazolidin-5-ylmethyl ester (4.05 g, 10 mM) gave the title product (4.93 g) of sufficient purity for further chemistry.

MS (ESP): 394 (MH^+) for $C_{23}H_{25}F_2N_3O_5S$ - $C_4H_8CO_2$

(*5R*)-{3-[3,5-Difluoro-4-(*1RS*-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester

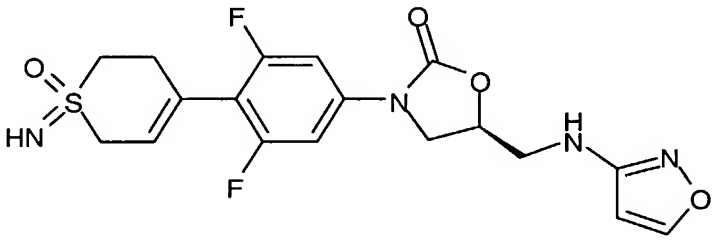


Using essentially the procedure of the appropriate intermediate for Example 1 but starting from (*5R*)-{3-[4-(3,6-dihydro-2*H*-thiopyran-4-yl)-3,5-difluoro-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester (4.93 g, 10 mM) gave the title product (4.56 g) after chromatography.

MS (Negative ESP): 554 ($M-H^-$) for $C_{23}H_{25}F_2N_3O_6S$ + HCOOH

NMR (DMSO-d_6) δ: 1.48 (s, 9H); 2.40 (dm, 1H); 2.81 (br m, 1H); 2.96 (td, 1H); 3.11 (dt, 1H); 3.40 (dd, 1H); 3.68 (dm, 1H); 3.87 (dd, 1H); 3.98 (dd, 1H); 4.21 (t, 1H); 4.28 (dd, 1H); 5.01 (m, 1H); 5.73 (br, 1H); 6.85 (d, 1H); 7.35 (d, 2H); 8.80 (d, 1H).

Example 9: (*5S*)-3-[3,5-Difluoro-4-(*1RS*-1-imino-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-ylaminomethyl)-oxazolidin-2-one

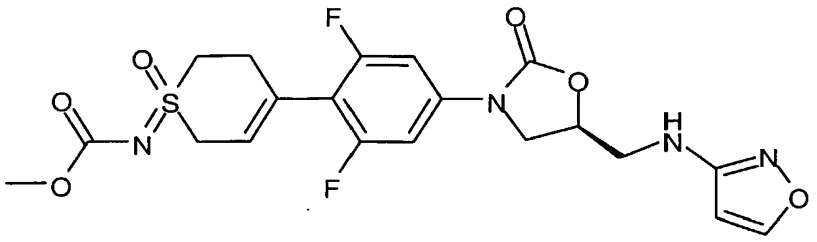


Using essentially the procedure of Example 3 , but starting from (*5R*)-{3-[3,5-difluoro-4-(*1RS*-1-imino-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester (150 mg, 0.21 mM) gave the title product (119 mg) as its TFA salt after precipitation from dichloromethane / diethyl ether. The free base may be prepared by distributing the salt between ethyl acetate and dilute aqueous ammonia, and evaporation of the organic layer.

MS (ESP): 425 (MH^+) for $C_{18}H_{18}F_2N_4O_4S$

NMR (DMSO-d_6) δ: 2.17 (s, 3H); 2.49 (overlapped by DMSO, ~6H); 2.95 (br m, 2H); 3.44 (d, 2H); 3.81 (dd, 1H); 4.15 (overlapping m, 3H); 4.65 (br, 2H); 4.90 (m, 1H); 5.85 (br, 1H); 5.97 (d, 1H); 6.76 (s, 2H); 7.36 (d, 2H); 8.31 (d, 1H); 3 exchangeables not seen.

Example 10: (5*S*)-(4-{2,6-Difluoro-4-[5-(isoxazol-3-ylaminomethyl)-2-oxo-oxazolidin-3-yl]-phenyl}-*1RS*-1-oxo-3,6-dihydrothiopyran-1-ylidene)-carbamic acid methyl ester



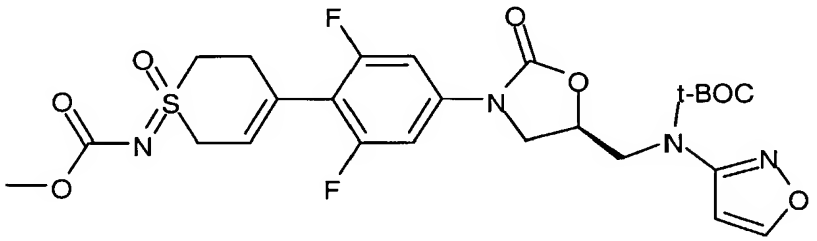
Using essentially the procedure of Example 3 but starting from (5*R*)-[4-(4-{5-[(*tert*-butoxycarbonyl-isoxazol-3-yl-amino)-methyl]-2-oxo-oxazolidin-3-yl}-2,6-difluoro-phenyl)-*1RS*-1-oxo-3,6-dihydrothiopyran-1-ylidene]-carbamic acid methyl ester (130 mg, 0.22 mM) gave the title compound (100 mg) after chromatography on a 10 g silica Mega Bond Elut® column, eluting with a gradient increasing in polarity from 0 to 5% methanol in dichloromethane and combining relevant fractions.

MS (Negative ESP): 527 ($M-H^-$) for $C_{20}H_{20}F_2N_4O_6S$ + HCOOH

NMR (DMSO-d_6) δ: 2.84 (br, 2H); 3.43 (t, 2H); 3.58 (s, 3H); 3.72 (t, 2H); 3.81 (dd, 1H); 4.16 (t, 1H); 4.27 (dm, 1H); 4.45 (dm, 1H); 4.90 (m, 1H); 5.80 (t, 1H); 6.00 (d, 1H); 6.51 (t, 1H); 7.37 (d, 2H); 8.38 (d, 1H).

The intermediate for this compound was prepared as follows

(5*R*)-[4-(4-{5-[(*tert*-Butoxycarbonyl-isoxazol-3-yl-amino)-methyl]-2-oxo-oxazolidin-3-yl}-2,6-difluoro-phenyl)-*1RS*-1-oxo-3,6-dihydrothiopyran-1-ylidene]-carbamic acid methyl ester

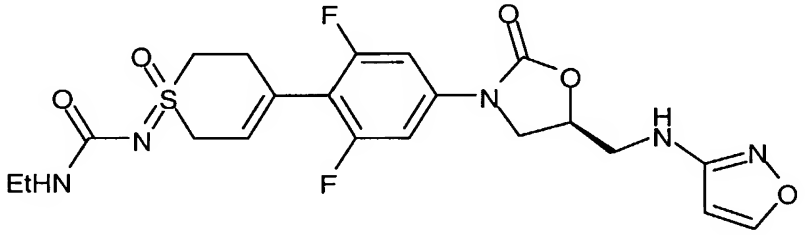


(5*R*)-{3-[3,5-Difluoro-4-(*1RS*-1-imino-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester (free base, 157 mg, 0.3 mM) was dissolved in tetrahydrofuran (5 ml), treated with triethylamine (145 mg, 1.44 mM), and stirred at ambient temperature. Methyl chloroformate (122 mg, 1.3 mM) was added

dropwise, and the whole stirred for 2 hours. The mixture was diluted with saturated sodium bicarbonate (20 ml) and ethyl acetate (20 ml), the organic layer separated, dried (magnesium sulfate) and evaporated to give title compound (130 mg), sufficiently pure for further chemistry.

MS (Negative ESP): 581 ($M-H^-$) for $C_{25}H_{28}F_2N_4O_8S$

Example 11: (*5S*)-1-(4-{2,6-Difluoro-4-[5-(isoxazol-3-ylaminomethyl)-2-oxo-oxazolidin-3-yl]-phenyl}-*1RS*-1-oxo-3,6-dihydrothiopyran-1-ylidene)-3-ethyl-urea



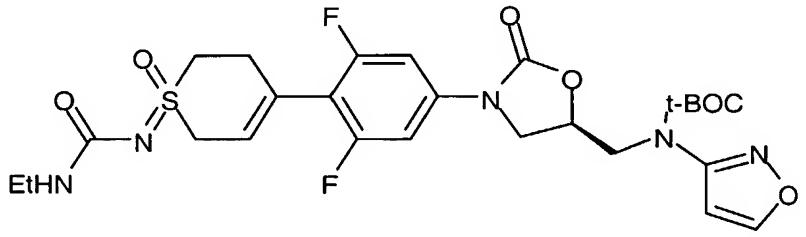
Using essentially the procedure of Example 3 but starting from (*5R*)-{3-[4-(1-ethyl-carbamoylimino-*1RS*-1-oxo-3,6-dihydrothiopyran-4-yl)-3,5-difluoro-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester (130 mg, 0.22 mM) gave the title compound (120 mg) after chromatography

MS (Negative ESP): 540 ($M-H^-$) for $C_{21}H_{23}F_2N_5O_5S$ + HCOOH

NMR (DMSO-d_6) δ: 0.99 (t, 3H); 2.80 (br, 2H); 2.99 (quintet, 2H); 3.43 (t, 2H); 3.61 (m, 2H); 3.80 (dd, 1H); 4.15 (t overlapping m, 2H); 4.37 (dm, 1H); 4.90 (m, 1H); 5.77 (t, 1H); 5.99 (d, 1H); 6.51 (t, 1H); 6.83 (t, 1H); 7.35 (d, 2H); 8.38 (d, 1H).

The intermediate for this compound was prepared as follows

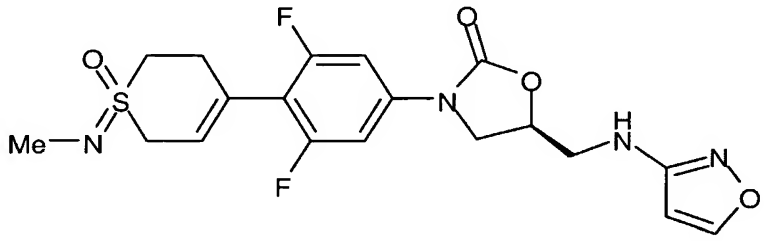
(*5R*)-{3-[4-(1-Ethylcarbamoylimino-*1RS*-1-oxo-3,6-dihydrothiopyran-4-yl)-3,5-difluoro-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester



(*5R*)-{3-[3,5-Difluoro-4-(*1RS*-1-imino-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester (free base, 157 mg, 0.3 mM) was dissolved in tetrahydrofuran (5 ml) under nitrogen at ambient temperature, treated dropwise with ethyl isocyanate (42 mg, 0.59 mM) and stirred for 18 hours. Solvent was evaporated to give title compound (130 mg), sufficiently pure for further chemistry.

MS (Negative ESP): 640 ($M-H^-$) for $C_{26}H_{31}F_2N_5O_7S$

Example 12: (*5S*)-3-[3,5-Difluoro-4-(*1RS*-1-methylimino-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-ylaminomethyl)-oxazolidin-2-one



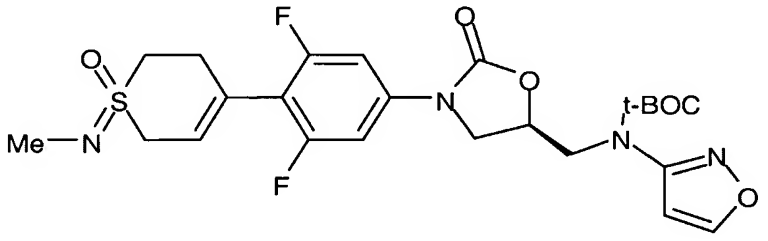
Using essentially the procedure of Example 3 but starting from (*5R*)-{3-[3,5-difluoro-4-(*1RS*-1-methylimino-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester (59 mg, 0.13 mM) gave the title compound (37 mg) after chromatography, contaminated with ~10% of C-alkylated congener.

MS (Negative ESP): 483 ($M-H^-$) for $C_{19}H_{20}F_2N_4O_4S$ + HCOOH

NMR ($CDCl_3$) δ: 2.80 (s, 3H); 2.84 (br, 2H); 3.20 (t, 2H); 3.55 (m, 1H); 3.66 (m, 1H); 3.77 (dd overlapping m, 2H); 3.86 (dd, 1H); 3.97 (t, 1H); 4.40 (t, 1H); 4.90 (m, 1H); 5.67 (t, 1H); 5.80 (d, 1H); 7.09 (d, 2H); 8.00 (d, 1H).

The intermediate for this compound was prepared as follows:

(*5R*)-{3-[3,5-Difluoro-4-(*1RS*-1-methylimino-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester



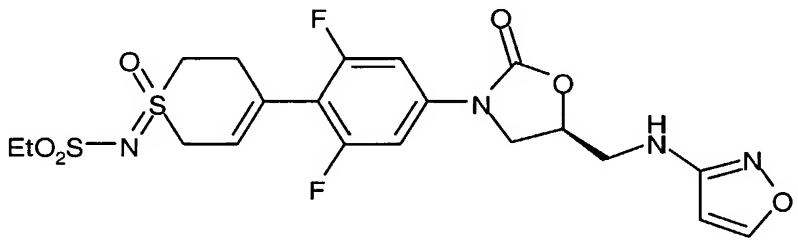
(*5R*)-{3-[3,5-Difluoro-4-(*1RS*-1-imino-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester (free base, 157 mg, 0.3 mM) was dissolved in tetrahydrofuran (5 ml) under nitrogen at ambient temperature, and treated with sodium hydride (50% in oil, 30 mg, 0.63 mM). After stirring for 10 minutes, iodomethane (228 mg, 1.61 mM) was added, and stirring continued for 1 hour.

Further sodium hydride (60 mg, 1.25 mM) and iodomethane (228 mg, 1.61 mM) was added and stirring continued for 1 hour.

The mixture was diluted with saturated sodium bicarbonate (20 ml) and ethyl acetate (20 ml), and the organic layer separated, dried (magnesium sulfate) and evaporated to give a gum which was purified by chromatography on a 10 g silica Mega Bond Elut® column, eluting with a gradient increasing in polarity from 0 to 100% ethyl acetate in dichloromethane. Relevant fractions were combined to give title product, contaminated with C-alkylated product.

MS (ESP): 539 (MH^+) for $C_{24}H_{28}F_2N_4O_6S$

Example 13: (*5S*)-Ethanesulfonic acid (4-{2,6-difluoro-4-[5-(isoxazol-3-ylaminomethyl)-2-oxo-oxazolidin-3-yl]-phenyl}-*1RS*-1-oxo-3,6-dihydrothiopyran-1-ylidene)-amide

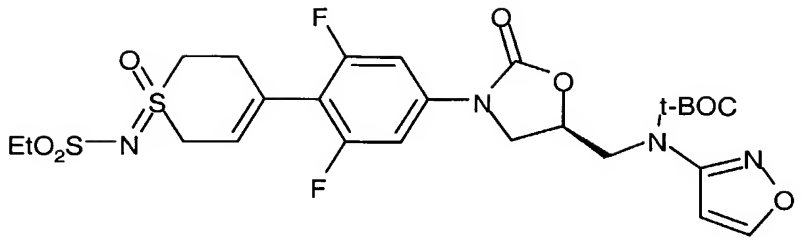


Using essentially the procedure of Example 3 but starting from (*5R*)-{3-[4-(*1RS*-1-ethanesulfonylimino-1-oxo-3,6-dihydrothiopyran-4-yl)-3,5-difluoro-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester (96 mg, 0.16 mM) gave the title compound (84 mg).

MS (ESP): 517 (MH^+) for $C_{20}H_{22}F_2N_4O_6S_2$

The intermediate for this compound was prepared as follows

(*5R*)-{3-[4-(*1RS*-1-Ethanesulfonylimino-1-oxo-3,6-dihydrothiopyran-4-yl)-3,5-difluoro-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester

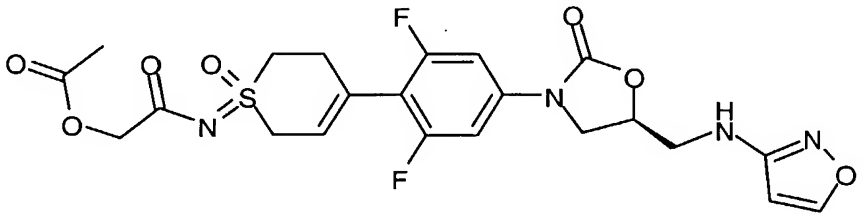


(*5R*)-{3-[3,5-Difluoro-4-(*1RS*-1-imino-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester (free base, 104 mg, 0.2 mM) was dissolved in dichloromethane (2 ml) under nitrogen, and treated with triethylamine (40 mg, 0.4 mM).

Ethanesulfonyl chloride (39 mg, 0.3 mM) was added, and the whole stirred for 18 hours. The mixture was diluted with dichloromethane (20 ml), washed with saturated sodium bicarbonate (20 ml), the organic layer separated, dried (magnesium sulfate) and evaporated. The residue was purified by chromatography on a 10 g silica Mega Bond Elut® column, eluting with a gradient increasing in polarity from 0 to 100% ethyl acetate in dichloromethane. Relevant fractions were combined to give title product (96 mg).

MS (ESP): 617 (MH^+) for $C_{25}H_{30}F_2N_4O_8S_2$

Example 14: Acetic acid (*5S*)-(4-{2,6-difluoro-4-[5-(isoxazol-3-ylaminomethyl)-2-oxo-oxazolidin-3-yl]-phenyl}-*1RS*-1-oxo-3,6-dihydrothiopyran-1-ylidenecarbamoyl)-methyl ester



Essentially the procedure of Example 3 was used, but starting from acetic acid (*5R*)-[4-(4-{5-[(*tert*-butoxycarbonyl-isoxazol-3-yl-amino)-methyl]-2-oxo-oxazolidin-3-yl}-2,6-difluoro-phenyl)-*1RS*-1-oxo-3,6-dihydrothiopyran-1-ylidenecarbamoyl]-methyl ester (460 mg, 0.74 mM). Crude trifluoroacetate salt was treated with ethyl acetate (25 ml), washed with sodium bicarbonate (5%, 20 ml), dried and evaporated to give the title product (310 mg).

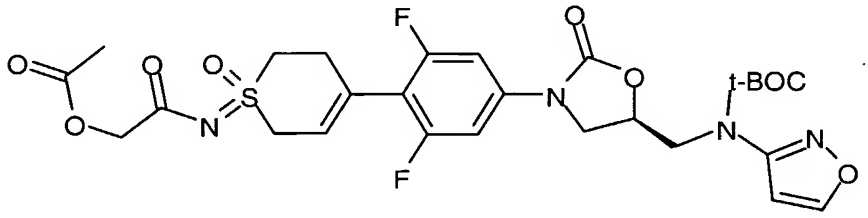
MS (Negative ESP): 523 ($M-H^-$) for $C_{22}H_{22}F_2N_4O_7S$

NMR (DMSO-d_6) δ: 2.06 (s, 3H); 2.84 (br, 2H); 3.44 (t, 2H); 3.78 (overlapping m, 3H);

4.16 (t, 1H); 4.30 (dm, 1H); 4.41 (dm, 1H); 4.47 (d, 1H); 4.55 (d, 1H); 4.91 (m, 1H); 5.77 (t, 1H); 6.00 (d, 1H); 6.52 (t, 1H); 7.36 (d, 2H); 8.38 (d, 1H).

The intermediate for this compound was prepared as follows:

Acetic acid (*5R*)-[4-(4-{5-[(*tert*-butoxycarbonyl-isoxazol-3-yl-amino)-methyl]-2-oxo-oxazolidin-3-yl}-2,6-difluoro-phenyl)-*1RS*-1-oxo-3,6-dihydrothiopyran-1-ylidenecarbamoyl]-methyl ester

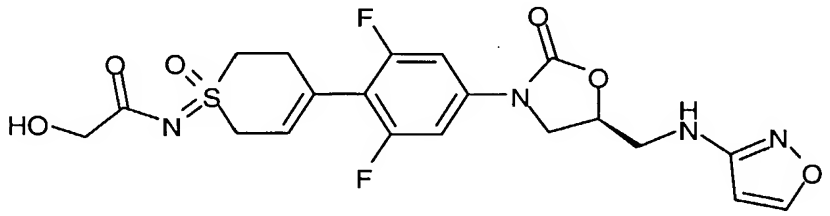


(*5R*)-{3-[3,5-difluoro-4-(*1RS*-1-imino-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester (480 mg, 0.916 mM) was stirred in a mixture of acetoxyacetyl chloride(6 ml) and saturated aqueous sodium bicarbonate (6 ml) at ambient temperature, and acetic anhydride (0.5 ml, excess) was added dropwise. After stirring 2 hours, the acetoxyacetyl chloride layer was separated, washed with sodium bicarbonate water, dried (magnesium sulfate) and evaporated. The residue was purified by chromatography on a 10 g silica Mega Bond Elut® column, and eluted with a gradient increasing in polarity from 0 to 100% acetoxyacetyl chloride in dichloromethane, then 0 to 10% methanol in dichloromethane. Relevant fractions were combined to give the title compound (485 mg) after chromatography.

MS (ESP): 625 (MH^+) for $C_{27}H_{30}F_2N_4O_9S$

NMR (DMSO-d_6) δ: 1.49 (s, 9H); 2.06 (s, 3H); 2.83 (br, 2H); 3.78 (t, 2H); 3.87 (dd, 1H); 3.98 (dd, 1H); 4.21 (t, 1H); 4.25 (dd, 1H); 4.30 (dm, 1H); 4.41 (dm, 1H); 4.47 (d, 1H); 4.54 (d, 1H); 5.03 (m, 1H); 5.79 (t, 1H); 6.85 (d, 1H); 7.37 (d, 2H); 8.81 (d, 1H).

Example 15: (5*S*)-*N*-(4-{2,6-Difluoro-4-[5-(isoxazol-3-yloxymethyl)-2-oxo-oxazolidin-3-yl]-phenyl}-*1RS*-1-oxo-3,6-dihydrothiopyran-1-ylidene)-2-hydroxy-acetamide

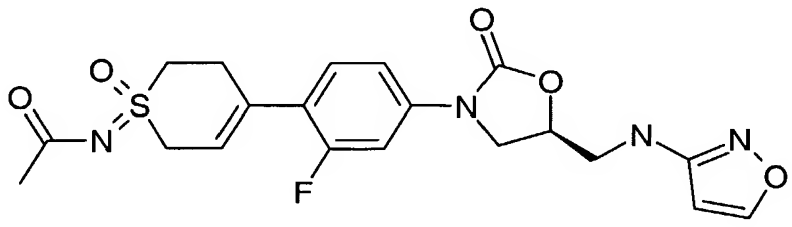


Acetic acid (*5S*)-(4-{2,6-difluoro-4-[5-(isoxazol-3-ylaminomethyl)-2-oxo-oxazolidin-3-yl]-phenyl}-*1RS*-1-oxo-3,6-dihydrothiopyran-1-ylidenecarbamoyl)-methyl ester (310 mg, 0.59 mM) was dissolved in tetrahydrofuran (5 ml), treated with saturated ammonia in methanol (10 ml) and stirred at ambient temperature for 18 hours. Solvent was evaporated, and the residue purified by chromatography on a 2 g silica Mega Bond Elut® column, and eluting with a gradient increasing in polarity from 0 to 10% methanol in dichloromethane. Relevant fractions gave the title compound (230 mg) after chromatography, contaminated with ~15% of the sulfoxime of Example 9.

MS (Negative ESP): 481 ($M-H^-$) for $C_{20}H_{20}F_2N_4O_6S$

NMR (DMSO-d_6) δ: 2.81 (br, 2H); 3.43 (t, 2H); 3.73 (t, 2H); 3.81 (dd, 1H); 3.90 (d, 2H); 4.15 (t, 1H); 4.29 (dd, 1H); 4.45 (dd, 1H); 4.76 (t, 1H); 4.90 (m, 1H); 5.77 (t, 1H); 5.99 (d, H); 6.52 (t, 1H); 7.37 (d, 2H); 8.38 (d, 1H).

Example 16: (5*S*)-3-[3-Fluoro-4-(*1RS*-1-(acetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one



(*5R*)-3-[3-Fluoro-4-(*1RS*-1-(acetylimino)-1-oxo-2,3-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl-*tert*-butoxycarbonyl)-oxazolidin-2-one (154mg, 0.28 mmol) was dissolved in dichloromethane (3ml) at 0 °C. Trifluoroacetic acid (3ml) was added, and the mixture stirred for 2 hours while warming to ambient temperature. The mixture was

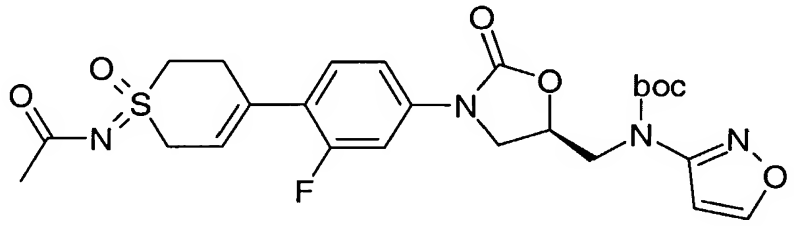
concentrated *in vacuo*, diluted with dichloromethane (10ml), and washed with 1M sodium bicarbonate, water, and brine, dried over sodium sulfate, and concentrated *in vacuo*. The residue was purified by flash chromatography using 3% methanol in dichloromethane as eluent. Relevant fractions were combined to give the title compound (64mg).

MS(APCI-pos): 449 (MH^+) for $C_{20}H_{21}FN_4O_5S$

NMR (DMSO-d_6) δ: 1.95 (s, 3H); 2.93 (m, 2H); 3.43 (m, 2H); 3.69 (m, 2H); 3.81 (dd, 1H); 4.15 (t, 1H); 4.20 (dd, 1H); 4.37 (dd, 1H); 4.88 (m, 1H); 5.84 (t, 1H); 5.98 (s, 1H); 6.54 (t, 1H); 7.32 (dd, 1H); 7.38 (t, 1H); 7.51 (dd, 1H); 8.38 (d, 1H).

The intermediates for this compound were prepared as follows:

(*5R*)-3-[3-Fluoro-4-(*1RS*-1-(acetylimino)-1-oxo-2,3-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl-*tert*-butoxycarbonyl)-oxazolidin-2-one

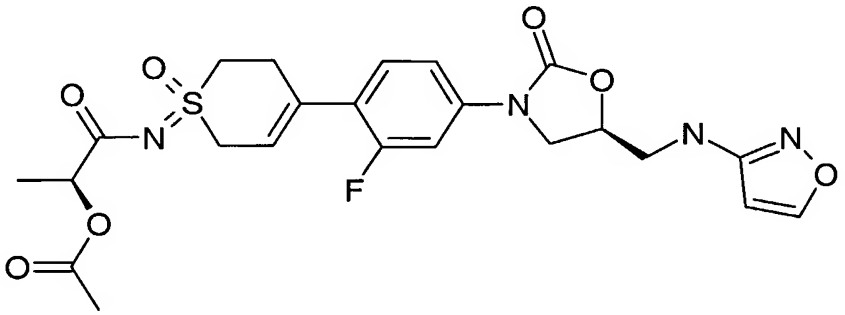


Example 2, ((*5R*)-3-[3-Fluoro-4-(*1RS*-1-imino-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl-*tert*-butoxycarbonyl)-oxazolidin-2-one mesitylene sulfonate salt) (200mg, 0.28 mmol) was dissolved in dichloromethane (2ml) and pyridine (0.5ml). The mixture was cooled to ⁻20 °C and a solution of acetic anhydride (53 µL, 0.57mmol) in dichloromethane (2ml) was added dropwise. The mixture was stirred for 5 hours while warming to ambient temperature. The reaction was concentrated *in vacuo*, diluted with ethyl acetate (20ml) and water (20ml). The layers were separated and the aqueous layer was extracted with ethyl acetate (3x20ml). The combined organic fractions were washed with 1N hydrochloric acid, water, and brine, dried over magnesium sulfate, and concentrated *in vacuo*. The residue was purified by flash chromatography with 1% methanol in dichloromethane as the eluent. Relevant fractions were combined to give the title compound (154mg).

MS(APCI-pos): 449 (MH^+ - BOC) for $C_{25}H_{29}FN_4O_7S$

NMR (DMSO-d_6) δ: 1.51 (s, 9H); 1.99 (s, 3H); 2.97 (br s, 2H); 3.72 (m, 2H); 3.89 (m, 1H); 4.02 (dd, 1H); 4.26 (overlapping m, 3H); 4.40 (br d, 1H); 5.04 (m, 1H); 5.88 (s, 1H); 6.89 (s, 1H); 7.38 (d, 1H); 7.43 (t, 1H); 7.53 (dd, 1H); 8.84 (s, 1H).

Example 17: (*5S*)-3-[3-Fluoro-4-(*1RS*-1-(*2S*-methyl-*2S*-acetoxyacetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one



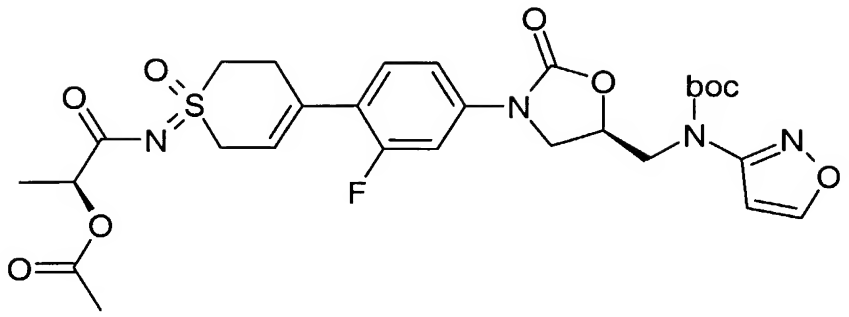
Essentially the procedure from Example 16 was used, but starting with (*5R*)-3-[3-Fluoro-4-(*1RS*-1-(*2S*-methyl-*2S*-acetoxyacetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl-*tert*-butoxycarbonyl)-oxazolidin-2-one (295mg, 0.48mmol). The crude product was purified by flash chromatography using 1.5% methanol in dichloromethane as eluent. Relevant fractions were combined giving the title compound (142mg).

MS(APCI-pos): 521 (MH^+) for $C_{23}H_{25}FN_4O_7S$

NMR (DMSO-d_6) δ: 1.38 (t, 3H); 2.03 (d, 3H); 2.97 (m, 2H); 3.46 (m, 2H); 3.77 (m, 1H); 3.84 (t, 2H); 4.18 (t, 1H); 4.31 (overlapping m, 2H); 4.45 (dm, 1H); 4.86 (q, 1H); 4.92 (m, 1H); 5.83 (m, 1H): 6.02 (s, 1H); 6.57 (t, 1H); 7.36 (t, 1H) 7.39 (m, 1H); 7.54 (d, 1H); 8.41 (s, 1H).

Intermediates for this compound were made as follows:

(*5R*)-3-[3-Fluoro-4-(*1RS*-1-(*2S*-methyl-*2S*-acetoxyacetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl-*tert*-butoxycarbonyl)-oxazolidin-2-one

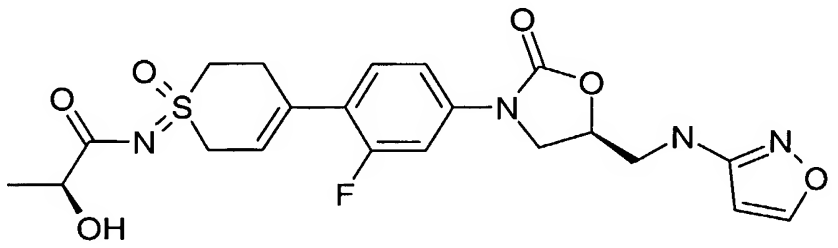


Prepared using essentially the same procedure as the appropriate intermediate in Example 16 but acylating the mesitylene sulfonate salt (400mg, 0.57mmol) with (S)-(-)-2-acetoxypropionyl chloride (164 μL, 1.13mmol). Flash chromatography with 1% methanol in dichloromethane as eluent gave the title compound (362mg).

MS(APCI-pos): 521 (MH^+- BOC) for $C_{28}H_{33}FN_4O_9S$

NMR (DMSO-d_6) δ: 1.38 (t, 3H); 1.50 (s, 9H); 2.03 (d, 3H); 2.97 (m, 2H); 3.83 (overlapping m, 2H); 4.01 (dd, 1H); 4.28 (overlapping m, 3H); 4.44 (dm, ~1H); 4.86 (m, 1H); 5.04 (m, 1H); 5.85 (m, 1H); 6.89 (br s, 1H); 7.40 (m, 2H); 7.53 (d, 1H); 8.84 (s, 1H).

Example 18: (*5S*)-3-[3-Fluoro-4-(*1RS*-1-(*2S*-methyl-*2S*-hydroxyacetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one



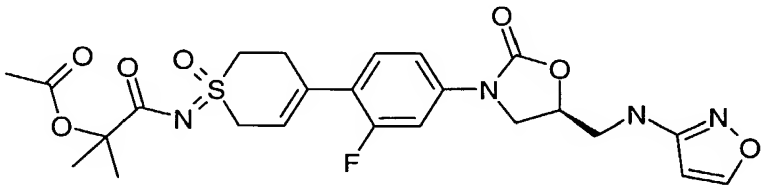
(*5S*)-3-[3-Fluoro-4-(*1RS*-1-(*2S*-methyl-*2S*-acetoxyacetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one (Example 17) (70mg, 0.13mmol) was dissolved in methanol (10ml) and cooled to 0 °C. Potassium carbonate (catalytic amount) was added and the mixture stirred at 0 °C. After 6 hours, water (10ml) was added and the volatiles were removed *in vacuo*. The residue was diluted with ethyl acetate (10ml) and water (5ml). The aqueous layer was extracted with ethyl acetate (3x10ml). The combined organics were washed with brine, dried over sodium sulfate, and concentrated *in vacuo*. The crude

residue was purified by flash chromatography using 100% ethyl acetate as the eluent. The relevant fractions were combined giving the title compound (47mg).

MS(APCI-pos): 479 (MH^+) for $C_{21}H_{23}FN_4O_6S$

NMR (DMSO-d_6) δ: 1.23 (dd, 3H); 2.98 (m, 2H); 3.46 (m, 2H); 3.73 (t, 1H); 3.78 (m, 1H); 3.83 (dd, 1H); 4.03 (m, 1H); 4.18 (t, 1H); 4.28 (dm, 1H); 4.45 (qm, 1H); 4.73 (t, 1H); 4.91 (m, 1H); 5.83 (q, 1H); 6.02 (s, 1H); 6.57 (t, 1H); 3.37 (overlapping m, 2H); 7.54 (dd, 1H); 8.41 (s, 1H).

Example 19: (*5S*)-3-[3-Fluoro-4-(*1RS*-1-(2,2-dimethyl-2-acetoxyacetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one



Essentially the same procedure was used as Example 16, but starting from (*5R*)-3-[3-fluoro-4-(*1RS*-1-(2,2-dimethyl-2-acetoxyacetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl-*tert*-butyoxycarbonyl)-oxazolidin-2-one (211mg, 0.33mmol). The crude product was purified by flash chromatography with 1.5% methanol in dichloromethane as eluent. The relevant fractions were combined giving the title compound (100mg).

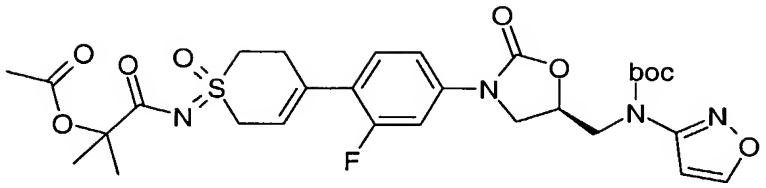
MS(APCI-pos): 535 (MH^+) for $C_{24}H_{27}FN_4O_7S$

NMR (DMSO-d_6) δ: 1.45 (s, 6H); 1.93 (s, 3H); 2.96 (m, 2H); 3.46 (overlapping m with H_2O, 2H); 3.77 (m, 2H); 3.84 (t, 1H); 4.18 (t, 1H); 4.26 (br d, 1H); 4.34 (dd, 1H); 4.91 (m, 1H); 5,82 (br s, 1H); 6.02 (s, 1H): 6.57 (t, 1H); 7.36 (d, 1H); 7.41 (t, 1H); 7.54 (d, 1H); 8.41 (s, 1H).

Intermediates for this compound were made as follows:

(*5R*)-3-[3-Fluoro-4-(*1RS*-1-(2,2-dimethyl-2-acetoxyacetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl-*tert*-butyoxycarbonyl)-

oxazolidin-2-one

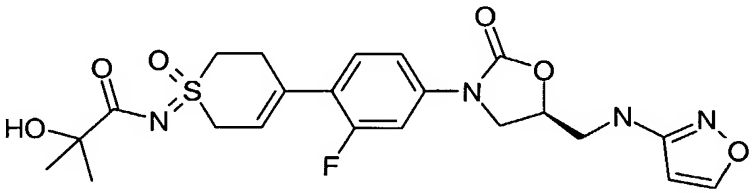


Using essentially the same procedure as the appropriate intermediate from Example 16, the mesitylene sulfonate salt (Example 2) (400mg, 0.57mmol) was acylated with 2-acetoxyisobutyrylchloride (164μL, 1.13mmol). Purification of the crude product by flash chromatography using 1% methanol in dichloromethane as eluent and combination of the relevant fractions gave the title compound (362mg).

MS(ES-pos): 635 (MH^+) for $C_{29}H_{35}FN_4O_9S$

NMR (DMSO-d_6) δ: 1.46 (d, 6H,); 1.50 (s, 9H); 1.93 (s, 3H); 2.97 (m, 2H); 3.78 (m, 2H); 3.89 (m, 1H); 4.01 (dd, 1H); 4.28 (overlapping m, 4H); 5.04 (m, 1H); 5.83 (br s, 1H); 6.89 (br s, 1H); 7.37 (d, 1H); 7.43 (t, 1H): 7.53 (d, 1H); 8.84 (s, 1H).

Example 20: (*5S*)-3-[3-Fluoro-4-(*1RS*-1-(2,2-dimethyl-2-hydroxyacetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one

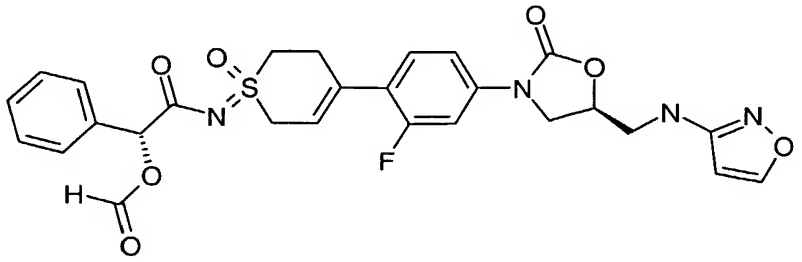


Essentially the same procedure was used as Example 18, but starting from (*5S*)-3-[3-Fluoro-4-(*1RS*-1-(2,2-dimethyl-2-acetoxyacetylimino)-1-oxo-2,3-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one (Example 19)(160mg, 0.3mmol). Crude product was purified on the Jones Flashmaster using 100% ethyl acetate as the eluent. Relevant fractions were combined giving the title compound (44mg).

MS(APCI-pos): 493 (MH^+) for $C_{22}H_{25}FN_4O_6S$

NMR (DMSO-d_6) δ: 1.27 (d, 6H); 2.98 (m, 2H); 3.46 (m, 2H); 3.76 (m, 2H); 3.83 (t, 1H); 4.18 (t, 1H); 4.28 (br d, 1H); 4.46 (dd, 1H); 4.53 (s, 1H); 4.91 (m, 1H); 5.84 (m, 1H); 6.02 (s, 1H); 6.57 (t, 1H); 7.36 (m, 2H); 7.53 (d, 1H); 8.41 (s, 1H).

Example 21: (5*S*)-3-[3-Fluoro-4-(1*RS*-1-(2*R*-phenyl-2*R*-formyloxyacetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one



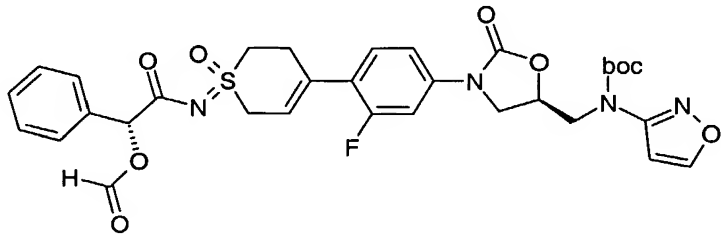
Essentially the same procedure was used as Example 16, but starting from (5*R*)-3-[3-Fluoro-4-(1*RS*-1-(2*R*-phenyl-2*R*-formyloxyacetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl-*tert*-butoxycarbonyl)-oxazolidin-2-one (287mg, 0.43mmol). Crude product was purified by flash chromatography using 1.5% methanol in dichloromethane as eluent. Relevant fractions were combined giving the title compound (163mg).

MS(APCI-pos): 569 (MH^+) for $C_{27}H_{25}FN_4O_7S$

NMR ($DMSO-d_6$) δ: 2.68 (m, 1H); 2.81 (m, 1H); 2.90 (dm, 2H); 3.78 (m, 2H); 3.85 (t, 2H); 4.19 (t, 1H); 4.29 (br t, 1H); 4.40 (tm, 1H); 4.92 (m, 1H); 5.91 (d, 1H); 6.02 (s, 1H); 6.58 (m, 1H); 7.22 (t, 1H); 7.34 (m, 4H); 7.49 (m, 2H); 7.74 (d, 1H); 8.38 (d, 1H); 8.42 (s, 1H).

The intermediates for this compound were prepared as follows:

(5*R*)-3-[3-Fluoro-4-(1*RS*-1-(2*R*-phenyl-2*R*-formyloxyacetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl-*tert*-butoxycarbonyl)-oxazolidin-2-one



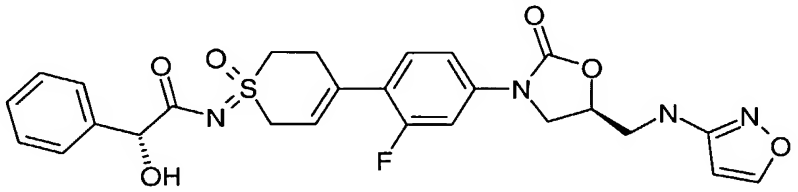
Using essentially the same procedure as the appropriate intermediate from Example 16, the mesitylene sulfonate salt (Example 2) (400mg, 0.57mmol) was acylated with (R)-(-)-formylmandeloyl chloride (176μl, 1.13mmol). The crude product was purified by flash chromatography using 1% methanol in dichloromethane as eluent. The relevant fractions

were pooled giving the title compound (437mg).

MS(APCI-pos): 569 (MH^+- BOC) for $C_{32}H_{33}FN_4O_9S$

NMR (DMSO-d_6) δ: 1.51 (s, 9H); 2.70 (m, 1H); 2.81 (m, 1H); 2.91 (m, 1H); 3.78 (m, 2H); 3.91 (dd, 1H); 4.01 (dd, 1H); 4.27 (overlapping m, 3H); 4.41 (tm, 1H); 5.05 (m, 1H); 5.77 (m, 1H); 5.91 (d, 1H); 6.89 (m, 1H); 7.34 (m, 4H); 7.49 (overlapping m, 3H); 8.38 (s, 1H); 8.84 (s, 1H).

Example 22: (*5S*)-3-[3-Fluoro-4-(*1RS*-1-(*2R*-phenyl-*2R*-hydroxyacetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one

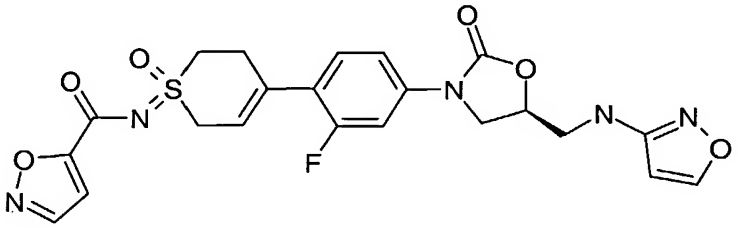


(*5S*)-3-[3-Fluoro-4-(*1RS*-1-(*2R*-phenyl-*2R*-formyloxyacetylimino)-1-oxo-2,3-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one (Example 21) (100mg, 0.18mmol) was dissolved in methanol (5ml)/ acetone (5ml). Solid sodium bicarbonate (13mg, 0.16mmol) was added and the mixture stirred at ambient temperature overnight. Mixture was diluted with ethyl acetate and water, the aqueous layer was extracted with ethyl acetate (3x); the combined organics were washed with brine and dried over sodium sulfate. Crude product was purified by recrystallization from hot ethanol giving the title compound (55mg).

MS(APCI-pos): 541 (MH^+) for $C_{26}H_{25}FN_4O_6S$

NMR (DMSO-d_6) δ: 2.62 (m, 1H); 2.78 (m, 1H); 2.88 (m, 2H); 3.47 (m, 2H); 3.73 (overlapping m, 2H); 3.85 (dd, 1H); 4.19 (t, 1H); 4.25 (br d, 1H); 4.40 (dm, 1H); 4.92 (m, 1H); 4.98 (t, 1H); 5.46 (dd, 1H); 5.76 (dm, 1H); 6.03 (s, 1H); 6.58 (t, 1H); 7.20 (overlapping m, 4H), 7.33 (dm, 1H); 7.42 (t, 2H); 7.53 (dm, 1H); 8.42 (s, 1H).

Example 23: (5*S*)-3-[3-Fluoro-4-(*1RS*-1-(2-isoxazol-5-yl-acetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one



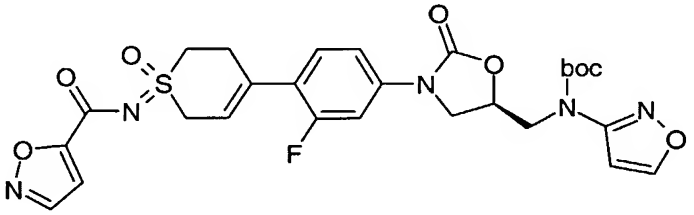
Essentially the same procedure was used as Example 16, but starting from (5*R*)-3-[3-Fluoro-4-(*1RS*-1-(2-isoxazol-5-yl-acetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl-*tert*-butoxycarbonyl)-oxazolidin-2-one (240mg, 0.48mmol). Crude product was purified by recrystallization from hot methanol giving the title product (10mg).

MS(APCI-pos): 502 (MH^+) for $C_{22}H_{20}FN_5O_6S$

NMR (DMSO-d_6) δ: 3.06 (t, 2H); 3.46 (t, 2H); 3.83 (dd, 1H); 3.93 (t, 2H); 4.18 (t, 1H); 4.47 (dd, 1H); 4.62 (dd, 1H); 4.91 (m, 1H); 5.92 (s, 1H); 6.02 (s, 1H); 6.57 (t, 1H); 7.04 (s, 1H); 7.35 (d, 1H); 7.42 (t, 1H); 7.74 (d, 1H); 8.41 (s, 1H); 8.73 (s, 1H).

Intermediates for this compound were made as follows:

(5*R*)-3-[3-Fluoro-4-(*1RS*-1-(2-isoxazol-5-yl-acetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl-*tert*-butoxycarbonyl)-oxazolidin-2-one



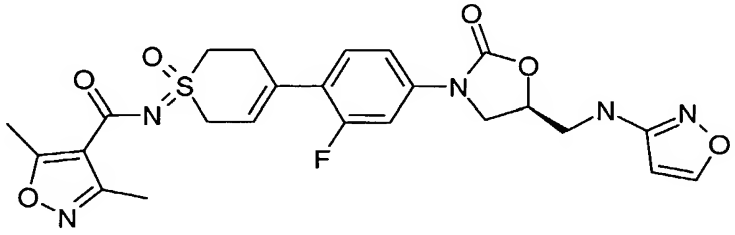
Using essentially the same procedure of the appropriate intermediate from Example 16, the mesitylene sulfonate salt of Example 2 (300mg, 0.42mmol) was acylated with isoxazole-5-carbonyl chloride (110mg, 0.84mmol). The crude product was purified by flash chromatography using 1% methanol in dichloromethane as eluent. The relevant fractions were combined giving the title compound (240mg).

MS(APCI-pos): 602 (MH^+- BOC) for $C_{27}H_{28}FN_5O_8S$

NMR (DMSO-d_6) δ: 1.50 (s, 9H); 3.06 (t, 2H); 3.89 (dd, 1H); 3.93 (t, 2H); 4.00 (dd, 1H);

4.42 (t, 1H); 4.29 (dd, 1H); 4.48 (dm, 1H); 4.62 (dm, 1H); 5.04 (m, 1H); 5.93 (t, 1H); 6.89 (br s, 1H); 7.04 (s, 1H); 7.37 (dd, 1H); 7.44 (t, 1H); 7.52 (dd, 1H); 8.74 (d, 1H); 8.84 (d, 1H).

Example 24: (*5S*)-3-[3-Fluoro-4-(*1RS*-1-(2-(3,5-dimethylisoxazol-4-yl)-acetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one



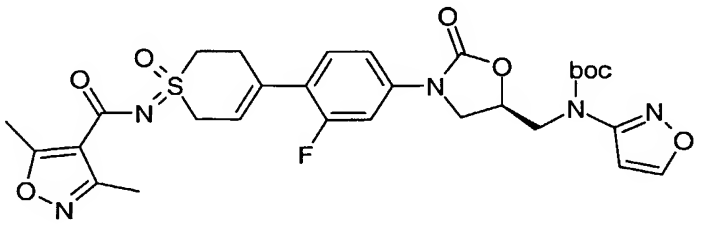
Essentially the procedure from Example 16 was used, but starting with (*5R*)-3-[3-Fluoro-4-(*1RS*-1-(2-(3,5-dimethylisoxazol-4-yl)-acetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl-*tert*-butoxycarbonyl)-oxazolidin-2-one (725mg, 1.15g). The crude product was purified on the Jones Flashmaster using a gradient of 2-10% methanol in dichloromethane. The relevant fractions were combined giving the title compound (450mg).

MS(APCI-pos): 530 (MH^+) for $C_{24}H_{24}FN_5O_6S$

NMR (DMSO-d_6) δ: 2.37 (s, 3H); 2.64 (s, 3H); 3.02 (m, 2H); 3.46 (t, 2H); 3.85 (m, 3H); 4.18 (t, 1H); 4.38 (dm, 1H); (4.56 (dm, 1H); 4.91 (m, 1H); 5.90 (t, 1H); 6.01 (d, 1H); 6.57 (t, 1H); 7.35 (dd, 1H); 7.41 (t, 1H); 7.54 (dd, 1H); 8.41 (d, 1H).

Intermediates for this compound were made as follows:

(*5R*)-3-[3-Fluoro-4-(*1RS*-1-(2-(3,5-dimethylisoxazol-4-yl)-acetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl-*tert*-butoxycarbonyl)-oxazolidin-2-one



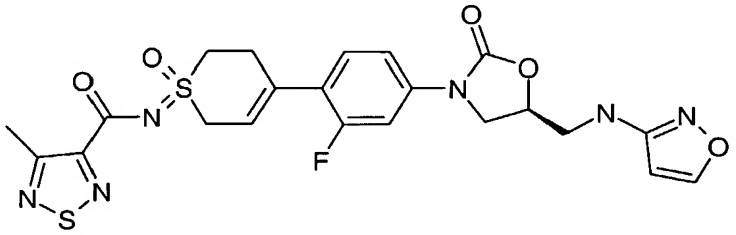
Using essentially the same procedure of the appropriate intermediate from Example 16, the

mesitylene sulfonate salt of Example 2 (1.0g, 1.41mmol) was acylated with 3,5-dimethylisoxazole-4-carbonyl chloride (452mg, 2.83mmol). The crude product was purified on the Jones Flashmaster using a gradient of 0-4% methanol in dichloromethane as eluent. The relevant fractions were combined giving the title compound (842mg).

MS(APCI-pos): 530 (MH^+- BOC) for $C_{29}H_{32}FN_5O_8S$

NMR ($DMSO-d_6$) δ: 1.50 (s, 9H); 2.37 (s, 3H); 2.64 (s, 3H); 3.03 (m, 2H); 3.85 (m, 3H); 4.01 (dd, 1H); 4.24 (t, 1H); 4.28 (dd, 1H); 4.38 (dm, 1H); 4.56 (dm, 1H); 5.04 (m, 1H); 5.91 (m, 1H); 6.89 (br s, 1H); 7.37 (dd, 1H); 7.43 (t, 1H); 7.52 (dd, 1H); 8.84 (dd, 1H).

Example 25: (5*S*)-3-[3-Fluoro-4-(*1RS*-1-(2-(4-methyl-1,2,3-thiadiazol-5-yl)-acetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one



Essentially the same procedure as Example 16 was used, but starting from (5*R*)-3-[3-Fluoro-4-(*1RS*-1-(2-(4-methyl-1,2,3-thiadiazol-5-yl)-acetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl-*tert*-butoxycarbonyl)-oxazolidin-2-one (680mg, 1.07mmol). The crude product was purified on the Jones Flashmaster using a gradient of 2-10% methanol in dichloromethane as eluent. The relevant fractions were combined giving the title compound (488mg).

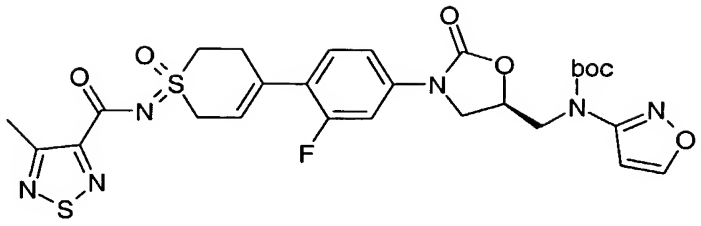
MS(APCI-pos): 533 (MH^+) for $C_{22}H_{21}FN_6O_5S_2$

NMR ($DMSO-d_6$) δ: 2.88 (s, 3H); 3.05 (m, 2H); 3.46 (dt, 2H); 3.83 (dd, 1H); 3.93 (t, 2H); 4.18 (t, 1H); 4.48 (dm, 1H); 4.63 (dm, 1H); 4.91 (m, 1H); 5.91 (t, 1H); 6.01 (d, 1H); 6.57 (t, 1H); 7.35 (dd, 1H); 7.41 (t, 1H); 7.54 (dd, 1H); 8.41 (d, 1H).

Intermediates for this compound were made as follows:

(5*R*)-3-[3-Fluoro-4-(*1RS*-1-(2-(4-methyl-1,2,3-thiadiazol-5-yl)-acetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl-*tert*-butoxycarbonyl)-

oxazolidin-2-one

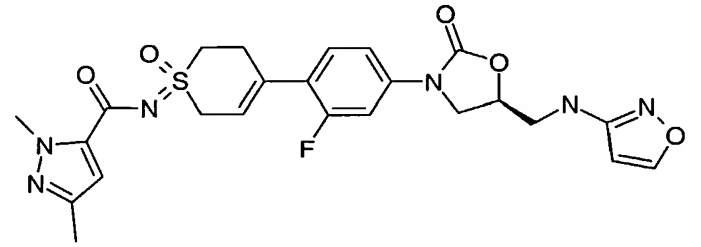


Using essentially the same procedure of the appropriate intermediate from Example 16, the mesitylene sulfonate salt of Example 2 (1.0g, 1.41mmol) was acylated with 4-methyl-1,2,3-thiadiazole-5-carbonyl chloride (460mg, 2.83mmol). The crude product was purified on the Jones Flashmaster using a gradient of 1-4% methanol in dichloromethane as eluent. The relevant fractions were combined giving the title compound (800mg).

MS(APCI-pos): 633 (MH^+) for $C_{27}H_{29}FN_6O_7S_2$

NMR (DMSO-d_6) δ: 1.50 (s, 9H); 2.88 (s, 3H); 3.06 (m, 2H); 3.88 (dd, 1H); 3.94 (t, 2H); 4.00 (dd, 1H); 4.23 (t, 1H); 4.29 (dd, 1H); 4.48 (dm, 1H); 4.63 (dm, 1H); 5.04 (m, 1H); 5.92 (m, 1H); 6.28 (br s, 1H); 7.37 (d, 1H); 7.43 (t, 1H); 7.53 (dd, 1H); 8.84 (d, 1H).

Example 26: (*5S*)-3-[3-Fluoro-4-(*1RS*-1-(2-(1,3-dimethyl-pyrazol-5-yl)-acetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one



Essentially the same procedure as Example 16 was used, but starting from (*5R*)-3-[3-Fluoro-4-(*1RS*-1-(2-(1,3-dimethyl-pyrazol-5-yl)-acetylimino)-1-oxo-2,3-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl-*tert*-butoxycarbonyl)-oxazolidin-2-one (690mg, 1.09mmol). Crude product was purified by flash chromatography using 2% methanol in dichloromethane as eluent. The relevant fractions were combined giving the title compound (493mg).

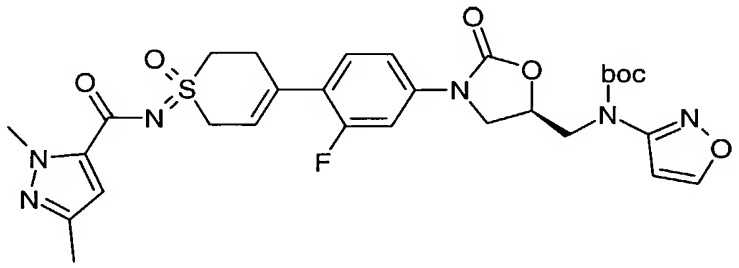
MS(APCI-pos): 529 (MH^+) for $C_{24}H_{25}FN_6O_5S$

NMR (DMSO-d_6) δ: 2.15 (s, 3H); 3.03 (m, 2H); 4.46 (t, 2H); 3.85 (m, 3H); 4.01 (s, 3H); 4.18 (t, 1H); 4.39 (dm, 1H); 4.57 (dm, 1H); 4.91 (m, 1H); 5.91 (t, 1H); 6.02 (d, 1H); 6.56

(overlapping m, 2H); 7.35 (dd, 1H); 7.41 (t, 1H); 7.54 (dd, 1H); 8.41 (d, 1H).

Intermediates for this compound were made as follows:

(5*R*)-3-[3-Fluoro-4-(*1RS*-1-(2-(1,3-dimethyl-pyrazol-5-yl)-acetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl-*tert*-butoxycarbonyl)-oxazolidin-2-one



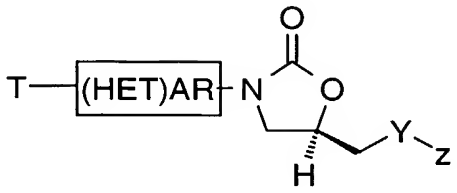
Using essentially the same procedure of the appropriate intermediate from Example 16, the mesitylene sulfonate salt of Example 2 (1.0g, 1.41mmol) was acylated with 1,3-dimethylpyrazole-5-carbonyl chloride (449mg, 2.83mmol). The crude product was purified by flash chromatography using 0.5 then 2% methanol in dichloromethane as eluent. The relevant fractions were combined giving the title compound (796 mg).

MS(ES-pos): 629 (MH^+) for $C_{29}H_{33}FN_6O_7S$

NMR (DMSO-d_6) δ: 1.50 (s, 9H); 2.16 (s, 3H); 3.04 (m, 2H); 3.85 (t, 2H); 3.89 (dd, 1H); 3.99 (d, 1H); 4.02 (s, 3H); 4.24 (t, 1H); 4.28 (dd, 1H); 4.40 (dm, 1H); 4.57 (dm, 1H); 5.04 (m, 1H); 5.92 (m, 1H); 6.56 (s, 1H); 6.89 (br s, 1H); 7.37 (dd, 1H); 7.43 (t, 1H); 7.53 (dd, 1H); 8.84 (dd, 1H).

CLAIMS

1. A compound of the formula (I), or a pharmaceutically-acceptable salt, or an in-vivo-hydrolysable ester thereof,

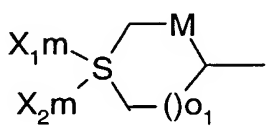


(I)

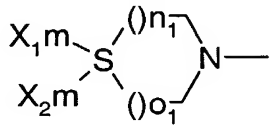
wherein:

T is selected from the groups in (TA) & (TB) belowCY;

(TA) T is selected from the following groups (TA1) and (TA2) :-



(TA1)



(TA2)

wherein :

in (TA1), $()o_1$ is 0 or 1 and represents a chain of carbon atoms (optionally substituted as defined for AR1) of length o_1 and M is a bond joining the adjacent carbon atoms, or M represents one or two carbon atoms, and defines a 4- to 7-membered monocyclic ring, which ring may optionally have one of

(i) one double bond between any two ring carbon atoms; or

(ii) a C1-C3 bridge connecting any two appropriate, non-adjacent ring carbon atoms, which bridge may optionally contain one heteroatom selected from oxygen or >NRc; or

(iii) a C2-C5 cyclic moiety including a ring carbon atom to define a spiro C2-C5 ring system, which ring may optionally contain one heteroatom selected from oxygen or >NRc; or

(iv) a C1-C4 bridge connecting adjacent carbon atoms to define a fused ring, wherein a C2-C4 bridge may optionally contain one heteroatom selected from oxygen or >NRc; wherein Rc is as defined hereinafter;

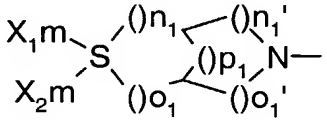
wherein in (TA2), ()n_1 and ()o_1 are independently 0, 1 or 2 and represent chains of carbon atoms (optionally substituted as defined for AR1) of length n_1 and o_1 respectively, and define a 4- to 8-membered monocyclic ring, which ring may optionally have one of

(i) a C1-C3 bridge connecting any two appropriate, non-adjacent ring carbon atoms, which bridge contains one heteroatom selected from oxygen or >NRc; or

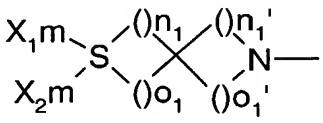
(ii) a C2-C5 cyclic moiety including a ring carbon atom to define a spiro C2-C5 ring system, which ring may optionally contain one heteroatom selected from oxygen or >NRc; or

(iii) a C1-C4 bridge connecting adjacent carbon atoms to define a fused ring, wherein a C2-C4 bridge may optionally contain one heteroatom selected from oxygen or >NRc; wherein Rc is as defined hereinafter;

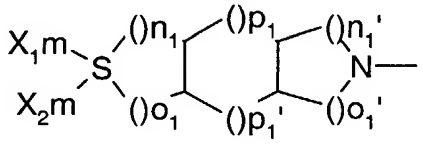
(TB) T is selected from the following groups (TB1) to (TB3) :-



(TB1)



(TB2)



(TB3)

wherein ()n_1, ()o_1, ()n_1', ()o_1', ()p_1 and ()p_1' represent chains of carbon atoms (optionally substituted as defined for AR1 hereinafter) of length n_1, o_1, n_1', o_1', p_1 and p_1' respectively, and are independently 0-2, with the proviso that in (TB1) and (TB2) the sum of n_1, o_1, n_1' and o_1' does not exceed 8 (giving a maximum ring size of 14 in (TB1) and 11 in (TB2)), and in (TB3) the sum of n_1, o_1, n_1', o_1', p_1 and p_1' does not exceed 6 (giving a maximum ring size of 12);

X_{1m} and X_{2m} taken together represent R_{2s}-$(E)_{ms}$-N=; or

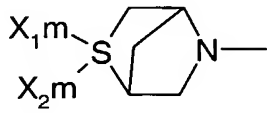
X_{1m} is O= and X_{2m} is R_{2s}-$(E)_{ms}$-N-, and vice versa;

wherein E is an electron withdrawing group selected from -SO_2-, -CO-, -O-CO-, -CO-O-, -CS-, -CON(R_s)-, -SO_2N(R_s)-, or E may represent a group of the formula R_{3s}-C(=N-O-R_{3s})-C(=O)-, wherein R_{3s} is H or as defined in R_{2s} at (i) below;

or, when E is -CON(R_s)- or -SO_2N(R_s)-, R_{2s} and R_s may link together to form a carbon chain which defines a 5- or 6-membered saturated, unsaturated or partially unsaturated ring linked via the N atom in E, which ring is optionally further substituted by an oxo substituent, and which ring may be optionally fused with a phenyl group to form a benzo-fused system, wherein the phenyl group is optionally substituted by up to three substituents independently selected from halo, cyano, (1-4C)alkyl and (1-4C)alkoxy;

ms is 0 or 1;

except, wherein in (TA1) (other than as defined in (i) – (iv) above), in (TA2) (other than as defined in (i) - (iii) above), or in (TB1) when TB1 is TB1b:



TB1b

and X_{1m} is O= and X_{2m} is R_{2s}-$(E)_{ms}$-N-, or vice versa,

R_{2s}-$(E)_{ms}$- may not be hydrogen, (1-4C)alkyl (optionally substituted as defined for R_p below), -C(=O)(1-4C)alkyl (optionally substituted as defined for R_p below), -C(=O)O(1-4C)alkyl (optionally substituted as defined for R_p below), -C(=O)NHR_p, or –C(=S)NHR_p,

wherein R_p is hydrogen, (1-4C)alkyl (optionally substituted with one or more halo, cyano, nitro, phenyl, (3-6C)cycloalkyl, OR_{p2}, C(=O)R_{p2}, OC(=O)R_{p2}, C(=O)OR_{p2}, S(=O)$_{mp}R_{p2}$, S(=O)$_{mp}NR_{p2}R_{p2}$, $NR_{p2}SO_2R_{p2}$, $NR_{p2}NSO_2R_{p2}R_{p2}$, NR_{p2}C(=O)R_{p2}, C(=O)$NR_{p2}R_{p2}$, $NR_{p2}R_{p2}$, oxo or oxime) or phenyl,

wherein R_{p2} is hydrogen, (1-4C)alkyl or phenyl,

wherein at each occurrence phenyl is optionally substituted with one or more halo, cyano, nitro, phenyl, (3-6C)cycloalkyl, OR_{p2}, C(=O)R_{p2}, OC(=O)R_{p2}, C(=O)OR_{p2}, S(=O)mpR_{p2}, S(=O)mp$NR_{p2}R_{p2}$, $NR_{p2}SO_2R_{p2}$, $NR_{p2}NSO_2R_{p2}R_{p2}$, NR_{p2}C(=O)R_{p2}, C(=O)$NR_{p2}R_{p2}$, or $NR_{p2}R_{p2}$,

and mp is 0, 1 or 2;

R_{2s} and R_s are independently selected from :

(i) hydrogen (except where E is -SO_2-or -O-CO-), or

(1-6C)alkyl {optionally substituted by one or more (1-4C)alkanoyl groups (including geminal

disubstitution) and/or optionally monosubstituted by cyano, cyano-imino, (1-4C)alkoxy, trifluoromethyl, (1-4C)alkoxycarbonyl, phenyl (optionally substituted as defined for AR1 hereinafter), optionally substituted heteroaryl group of the formula AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a or CY all as defined (and optionally substituted as defined) hereinafter, (1-4C)alkylS(O)$_q$- (q is 0, 1 or 2); and/or (with the proviso that where R_{2s} is -SO_2 or -O-CO- not on the first carbon atom of the (1-6C) alkyl chain) optionally substituted by one or more groups (including geminal disubstitution) each independently selected from hydroxy and fluoro, and/or optionally further substituted, by no more than one of each of, oxo, -NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl], (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino, N-(1-4C)alkyl-N-(1-6C)alkanoylamino, (1-4C)alkylS(O)$_p$NH- or (1-4C)alkylS(O)$_p$-((1-4C)alkyl)N- (p is 1 or 2)}; or

(ii) an optionally substituted aryl or optionally substituted heteroaryl group of the formula AR1, AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a or CY all as defined (and optionally substituted as defined) hereinafter;

or (where ms is 0 only);

(iii) cyano, -CO-NRvRw, -CO-NRv Rw', -SO_2-NRvRw, -SO_2-NRv Rw' [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl; Rw' is phenyl (optionally substituted as defined for AR1 hereinafter), or a heteroaryl group selected from AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a (optionally substituted as defined hereinafter)],

(1-4C)alkoxycarbonyl, trifluoromethyl, ethenyl, 2-(1-4C)alkylethenyl, 2-cyanoethenyl, 2-cyano-2-((1-4C)alkyl)ethenyl, 2-nitroethenyl, 2-nitro-2-((1-4C)alkyl)ethenyl, 2-((1-4C)alkylaminocarbonyl)ethenyl, 2-((1-4C)alkoxycarbonyl)ethenyl, 2-(AR1)ethenyl, 2-(AR2)ethenyl, or 2-(AR2a)ethenyl;

wherein Rc is selected from groups (Rc1) to (Rc5) :-

(Rc1) optionally substituted (1-6C)alkyl;

(Rc2) $R^{13}CO-$, $R^{13}SO_2-$ or $R^{13}CS-$

wherein R^{13} is selected from (Rc2a) to (Rc2e) :-

(Rc2a) AR1, AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a, CY;

(Rc2b) hydrogen, (1-4C)alkoxycarbonyl, trifluoromethyl, -NRvRw [wherein Rv is cyanoethenyl, 2-cyano-2-((1-4C)alkyl)ethenyl, 2-nitroethenyl, 2-nitro-2-((1-4C)alkyl)ethenyl, 2-((1-4C)alkylaminocarbonyl)ethenyl,

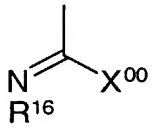
2-((1-4C)alkoxycarbonyl)ethenyl, 2-(AR1)ethenyl, 2-(AR2)ethenyl, 2-(AR2a)ethenyl;

(Rc2c) optionally substituted (1-10C)alkyl;

(Rc2d) $R^{14}C(O)O$(1-6C)alkyl wherein R^{14} is AR1, AR2, (1-4C)alkylamino (the (1-4C)alkyl group being optionally substituted by (1-4C)alkoxycarbonyl or by carboxy), benzyloxy-(1-4C)alkyl or (1-10C)alkyl {optionally substituted as defined for (Rc2c)};

(Rc2e) $R^{15}O$- wherein R^{15} is benzyl, (1-6C)alkyl {optionally substituted as defined for (Rc2c)}, CY, or AR2b;

(Rc3) hydrogen, cyano, 2-cyanoethenyl, 2-cyano-2-((1-4C)alkyl)ethenyl, 2-((1-4C)alkylaminocarbonyl)ethenyl, 2-((1-4C)alkoxycarbonyl)ethenyl, 2-nitroethenyl, 2-nitro-2-((1-4C)alkyl)ethenyl, 2-(AR1)ethenyl, 2-(AR2)ethenyl, or of the formula **(Rc3a)**



(Rc3a)

wherein X^{00} is $-OR^{17}$, $-SR^{17}$, $-NHR^{17}$and $-N(R^{17})_2$;

wherein R^{17} is hydrogen (when X^{00} is $-NHR^{17}$and $-N(R^{17})_2$), and R^{17} is (1-4C)alkyl, phenyl or AR2 (when X^{00} is $-OR^{17}$, $-SR^{17}$ and $-NHR^{17}$); and R^{16} is cyano, nitro, (1-4C)alkylsulfonyl, (4-7C)cycloalkylsulfonyl, phenylsulfonyl, (1-4C)alkanoyl and (1-4C)alkoxycarbonyl;

(Rc4) trityl, AR1, AR2, AR2a, AR2b, AR3, AR3a, AR3b;

(Rc5) RdOC(Re)=CH(C=O)-, RfC(=O)C(=O)-, RgN=C(Rh)C(=O)- or RiNHC(Rj)=CHC(=O)- wherein Rd is (1-6C)alkyl; Re is hydrogen or (1-6C)alkyl, or Rd and Re together form a (3-4C)alkylene chain; Rf is hydrogen, (1-6C)alkyl, hydroxy(1-6C)alkyl, (1-6C)alkoxy(1-6C)alkyl, -NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl], (1-6C)alkoxy, (1-6C)alkoxy(1-6C)alkoxy, hydroxy(2-6C)alkoxy, (1-4C)alkylamino(2-6C)alkoxy, di-(1-4C)alkylamino(2-6C)alkoxy; Rg is (1-6C)alkyl, hydroxy or (1-6C)alkoxy; Rh is hydrogen or (1-6C)alkyl; Ri is hydrogen, (1-6C)alkyl, AR1, AR2, AR2a, AR2b and Rj is hydrogen or (1-6C)alkyl;

CY is an optionally substituted cyclobutyl, cyclopentyl, cyclohexyl, cyclopentenyl or cyclohexenyl ring;

(HET)AR is a 5-6 membered aromatic or heteroaromatic ring, (i) when a 5-membered ring this may be a thiophene ring, comprising a single sulphur atom sited ortho to the nitrogen atom on the adjacent oxazolidinone ring, such a ring may have a single optional substituent

R1 as hereinafter defined sited ortho to the carbon atom on the adjacent sulfilimine/sulfoximine ring, (ii) when a 6-membered ring this may be a phenyl ring or comprise a single nitrogen atom sited ortho to the nitrogen atom on the adjacent oxazolidinone ring, such ring may be optionally substituted at one or both positions ortho to the carbon atom on the adjacent sulfilimine/sulfoximine ring by R1, where each

R1 is independently selected from hydrogen, halogen, methyl and methoxy, ethyl and ethoxy;

Y is -NR4- wherein R4 is hydrogen, or (1-6C)alkyl or -COOR5 wherein R5 is (1-6C) alkyl optionally substituted by one or more chlorine atoms; and

Z is a C5-C6 heteroaromatic ring joined to Y via a ring carbon atom, which ring is optionally substituted on an available carbon atom by 1 or 2 substituents independently selected from (1-4C)alkyl, amino, (1-4C)alkylamino, (1-4C)alkoxy and halogen, and/or on an available nitrogen atom (provided that the ring is not thereby quaternised) by (1-4C)alkyl.

2. A compound as claimed in claim 1, or a pharmaceutically-acceptable salt, or in-vivo hydrolysable ester thereof, wherein **Y** is -NR4- wherein R4 is (1-6C)alkyl or -COOR5 wherein R5 is (1-6C) alkyl optionally substituted by one or more chlorine atoms.

3. A compound as claimed in claim 1, or a pharmaceutically-acceptable salt, or in-vivo hydrolysable ester thereof,
wherein, X_{1m} and X_{2m} taken together represent R_{2s}-$(E)_{ms}$-N= .

4. A compound as claimed in claim 1, or a pharmaceutically-acceptable salt, or an in-vivo-hydrolysable ester thereof,
wherein :
in (TA1), $()o_1$ is 0 or 1 and represents a chain of carbon atoms (optionally substituted as defined for AR1) of length o_1 and M is a bond joining the adjacent carbon atoms, or M represents one or two carbon atoms, and defines a 4- to 7-membered monocyclic ring, which ring contains one of
(i) one double bond between any two ring carbon atoms; or
(ii) a C1-C3 bridge connecting any two appropriate, non-adjacent ring carbon atoms, which bridge may optionally contain one heteroatom selected from oxygen or >NRc; or

(iii) a C2-C5 cyclic moiety including a ring carbon atom to define a spiro C2-C5 ring system, which ring may optionally contain one heteroatom selected from oxygen or >NRc; or

(iv) a C1-C4 bridge connecting adjacent carbon atoms to define a fused ring, wherein a C2-C4 bridge may optionally contain one heteroatom selected from oxygen or >NRc; wherein Rc is as defined hereinafter;

wherein in (TA2), $()n_1$ and $()o_1$ are independently 0, 1 or 2 and represent chains of carbon atoms (optionally substituted as defined for AR1) of length n_1 and o_1 respectively, and define a 4- to 8-membered monocyclic ring, which ring contains one of

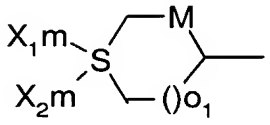
(i) a C1-C3 bridge connecting any two appropriate, non-adjacent ring carbon atoms, which bridge contains one heteroatom selected from oxygen or >NRc; or

(ii) a C2-C5 cyclic moiety including a ring carbon atom to define a spiro C2-C5 ring system, which ring may optionally contain one heteroatom selected from oxygen or >NRc; or

(iii) a C1-C4 bridge connecting adjacent carbon atoms to define a fused ring, wherein a C2-C4 bridge may optionally contain one heteroatom selected from oxygen or >NRc.

5. A compound of the formula (I) or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof wherein:

T is (TA1);



TA1

$\mathbf{X_{1m}}$ and $\mathbf{X_{2m}}$ taken together represent R_{2s}-(E)ms-N=, wherein E is an electron withdrawing group selected from SO2-, CO-, O-CO-, CO-O-, CS-, CON(R_s)-, SO2N(R_s)-, or E may represent a group of the formula R_{3s}-C(=N-O-R_{3s})-C(=O)-, wherein R_{3s} is H or as defined in R_{2s}(i) below; or

$\mathbf{X_{1m}}$ is O= and $\mathbf{X_{2m}}$ is R_{2s}-(E)ms-N-, and vice versa;

and R_{2s} and R_s may be linked as a 5- or 6-membered unsaturated or partially unsaturated ring;

ms is 0 or 1;

R_{2s} and R_s are independently selected from:

(i) hydrogen (except where E is SO2 or O-CO-), a (1-6C) alkyl group {optionally substituted by one or more (1-4C)alkanoyl groups (including geminal disubstitution) and/or optionally

monosubstituted by cyano, (1-4C)alkoxy, trifluoromethyl, (1-4C)alkoxycarbonyl, phenyl (optionally substituted as for AR defined herein after, heteroaryl(optionally substituted and defined as below),(1-4C)alkylS(O)$_q$- (q is 0, 1 or 2); or (with the proviso that where R_{2s} is SO2 or O-CO- not on the first carbon atom of the (1-6C) alkyl chain) optionally substituted by one or more groups (including geminal disubstitution) each independently selected from hydroxy and fluoro, and/or optionally monosubstituted by oxo, -NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl], (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino, N-(1-4C)alkyl-N-(1-6C)alkanoylamino, (1-4C)alkylS(O)$_p$NH- or (1-4C)alkylS(O)$_p$-((1-4C)alkyl)N- (p is 1 or 2)};

or

(ii) an optionally substituted aryl or heteroaryl group of the formula AR1, AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a, or CY all as hereinafter defined,

or where m=0 only,

(iii) cyano (1-4C)alkoxycarbonyl, trifluoromethyl, ethenyl, 2-(1-4C)alkylethenyl, 2-cyanoethenyl, 2-cyano-2-((1-4C)alkyl)ethenyl, 2-nitroethenyl, 2-nitro-2-((1-4C)alkyl)ethenyl, 2-((1-4C)alkylaminocarbonyl)ethenyl,

2-((1-4C)alkoxycarbonyl)ethenyl, 2-(AR1)ethenyl, 2-(AR2)ethenyl, or 2-(AR2a)ethenyl;

M is a bond joining the adjacent carbon atoms or represents one or two carbon atoms (each -CH2- or -CH-), the heterocyclic ring comprising M therefore has 5-7 ring atoms and may optionally have one or more of (i) one double bond between ring carbon atoms, (ii) a C1-C3 bridge connecting two ring carbon atoms and optionally containing a heteroatom selected from oxygen or nitrogen, and (iii) a C2-C5 cyclic moiety around a ring carbon atom;

o1 = 1;

except that, (other than when the heterocyclic ring comprising M is optionally substituted as defined in (i) – (iii) above) when X_{1m} is O= and X_{2m} is R_{2s}-(E)$_{ms}$-N-, or vice versa, R_{2s}-(E)$_{ms}$- may not be hydrogen, (1-4C)alkyl (optionally substituted as defined for R_p below), -C(=O)(1-4C)alkyl (optionally substituted as defined for R_p below), -C(=O)O(1-4C)alkyl (optionally substituted as defined for R_p below), -C(=O)NHR$_p$, or –C(=S)NHR$_p$, wherein R_p is hydrogen, (1-4C)alkyl (optionally substituted with one or more halo, cyano, nitro, phenyl, (3-6C)cycloalkyl, OR$_{p2}$, C(=O)R$_{p2}$, OC(=O)R$_{p2}$, C(=O)OR$_{p2}$, S(=O)$_{mp}$R$_{p2}$, S(=O)$_{mp}$NR$_{p2}$R$_{p2}$, NR$_{p2}$SO$_2$R$_{p2}$, NR$_{p2}$NSO$_2$R$_{p2}$R$_{p2}$, NR$_{p2}$C(=O)R$_{p2}$, C(=O)NR$_{p2}$R$_{p2}$, NR$_{p2}$R$_{p2}$,

oxo or oxime) or phenyl,

wherein R_{p2} is hydrogen, (1-4C)alkyl or phenyl,

wherein at each occurrence phenyl is optionally substituted with one or more halo, cyano, nitro, phenyl, (3-6C)cycloalkyl, OR_{p2}, $C(=O)R_{p2}$, $OC(=O)R_{p2}$, $C(=O)OR_{p2}$, $S(=O)mpR_{p2}$, $S(=O)mpNR_{p2}R_{p2}$, $NR_{p2}SO_2R_{p2}$, $NR_{p2}NSO_2R_{p2}R_{p2}$, $NR_{p2}C(=O)R_{p2}$, $C(=O)NR_{p2}R_{p2}$, or $NR_{p2}R_{p2}$,

mp is 0, 1 or 2;

(HET)AR is a 5-6 membered aromatic or heteroaromatic ring, (i) when a 5-membered ring this may be a thiophene ring, comprising a single sulphur atom sited ortho to the nitrogen atom on the adjacent oxazolidinone ring, such a ring may have a single optional substituent R1 as hereinafter defined sited ortho to the carbon atom on the adjacent sulfilimine/sulfoximine ring, (ii) when a 6-membered ring this may be a phenyl ring or comprise a single nitrogen atom sited ortho to the nitrogen atom on the adjacent oxazolidinone ring, such ring may be optionally substituted at one or both positions ortho to the carbon atom on the adjacent sulfilimine/sulfoximine ring by R1, where each

R1 is independently selected from hydrogen, halogen, methyl and methoxy, ethyl and ethoxy;

Y is -NR4- wherein R4 is hydrogen, or (1-6C)alkyl or -COOR5 wherein R5 is (1-6C) alkyl optionally substituted by one or more chlorine atoms;

Z is a C5-C6 heteroaromatic ring joined to Y via a ring carbon atom, which ring is optionally substituted on an available carbon atom by 1 or 2 substituents independently selected from (1-4C)alkyl, amino, (1-4C)alkylamino, (1-4C)alkoxy and halogen, and/or on an available nitrogen atom (provided that the ring is not thereby quaternised) by (1-4C)alkyl;

AR1 is an optionally substituted phenyl or optionally substituted naphthyl;

AR2 is an optionally substituted 5- or 6-membered, fully unsaturated (i.e with the maximum degree of unsaturation) monocyclic heteroaryl ring containing up to four heteroatoms independently selected from O, N and S (but not containing any O-O, O-S or S-S bonds), and linked via a ring carbon atom, or a ring nitrogen atom if the ring is not thereby quaternised;

AR2a is a partially hydrogenated version of AR2 (i.e. AR2 systems retaining some, but not the full, degree of unsaturation), linked via a ring carbon atom or linked via a ring nitrogen atom if the ring is not thereby quaternised;

AR2b is a fully hydrogenated version of AR2 (i.e. AR2 systems having no unsaturation), linked via a ring carbon atom or linked via a ring nitrogen atom;

AR3 is an optionally substituted 8-, 9- or 10-membered, fully unsaturated (i.e with the maximum degree of unsaturation) bicyclic heteroaryl ring containing up to four heteroatoms independently selected from O, N and S (but not containing any O-O, O-S or S-S bonds), and linked via a ring carbon atom in either of the rings comprising the bicyclic system;

AR3a is a partially hydrogenated version of AR3 (i.e. AR3 systems retaining some, but not the full, degree of unsaturation), linked via a ring carbon atom, or linked via a ring nitrogen atom if the ring is not thereby quaternised, in either of the rings comprising the bicyclic system;

AR3b is a fully hydrogenated version of AR3 (i.e. AR3 systems having no unsaturation), linked via a ring carbon atom, or linked via a ring nitrogen atom, in either of the rings comprising the bicyclic system;

AR4 is an optionally substituted 13- or 14-membered, fully unsaturated (i.e with the maximum degree of unsaturation) tricyclic heteroaryl ring containing up to four heteroatoms independently selected from O, N and S (but not containing any O-O, O-S or S-S bonds), and linked via a ring carbon atom in any of the rings comprising the tricyclic system;

AR4a is a partially hydrogenated version of AR4 (i.e. AR4 systems retaining some, but not the full, degree of unsaturation), linked via a ring carbon atom, or linked via a ring nitrogen atom if the ring is not thereby quaternised, in any of the rings comprising the tricyclic system; and

CY is an optionally substituted cyclobutyl, cyclopentyl, cyclohexyl, cyclopentenyl or cyclohexenyl ring.

6. A compound as claimed in claim 5 or pharmaceutically-acceptable salt or in-vivo hydrolysable ester thereof wherein: **Y** is -NR4- wherein R4 is (1-6C)alkyl or -COOR5 wherein R5 is (1-6C) alkyl optionally substituted by one or more chlorine atoms;

7. A compound as claimed in claim 5 or pharmaceutically-acceptable salt or in-vivo hydrolysable ester thereof wherein:

X_{1m} and X_{2m} taken together represent R_{2s}-(E)ms-N=.

8. A compound as claimed in claim 5 or pharmaceutically-acceptable salt or in-vivo hydrolysable ester thereof wherein:

M is a bond joining the adjacent carbon atoms or represents one or two carbon atoms (each -CH2- or -CH-), the heterocyclic ring comprising M therefore has 5-7 ring atoms and also has one or more of (i) one double bond between ring carbon atoms, (ii) a C1-C3 bridge connecting two ring carbon atoms and optionally containing a heteroatom selected from oxygen or nitrogen, and (iii) a C2-C5 cyclic moiety around a ring carbon atom;

9. A compound of the formula (I) as claimed in any one of claims 1 to 8, or a pharmaceutically acceptable salt, or in-vivo hydrolysable ester thereof, wherein:

when ms is 0, R_{2s} is selected from :

(i) hydrogen, a (1-6C)alkyl group {optionally monosubstituted by (1-4C)alkanoyl group, cyano, cyano-imino, (1-4C)alkoxy, trifluoromethyl, (1-4C)alkoxycarbonyl, phenyl (optionally substituted as for AR1 defined herein), optionally substituted heteroaryl group of the formula AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a or CY all as defined (and optionally substituted as defined) herein, (1-4C)alkylS(O)$_q$- (q is 0, 1 or 2); or optionally substituted by one or more fluoro groups (including geminal disubstitution); or optionally substituted by one or more hydroxy groups (excluding geminal disubstitution), and/or optionally further substituted, by no more than one of each of, oxo, -NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl], (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino, N-(1-4C)alkyl-N-(1-6C)alkanoylamino, (1-4C)alkylS(O)$_p$NH- or (1-4C)alkylS(O)$_p$-((1-4C)alkyl)N- (p is 1 or 2)}; or

(ii) an optionally substituted aryl or optionally substituted heteroaryl group of the formula AR1, AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a or CY all as defined (and optionally substituted as defined) herein; or

(iii) cyano, -CO-NRvRw, -CO-NRv Rw', -SO_2-NRvRw, -SO_2-NRv Rw' [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl; Rw' is phenyl (optionally substituted as for AR1 defined herein), or a heteroaryl group selected from AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a (optionally substituted as defined herein)], (1-4C)alkoxycarbonyl, trifluoromethyl; and wherein

when ms is 1, E is -CO- or -SO_2- and R_{2s} is selected from :

(i) (1-6C)alkyl {optionally monosubstituted by cyano, cyano-imino, (1-4C)alkoxy,

trifluoromethyl, (1-4C)alkoxycarbonyl, phenyl (optionally substituted as for AR1 defined herein), optionally substituted heteroaryl group of the formula AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a or CY all as defined (and optionally substituted as defined) herein, (1-4C)alkylS(O)$_q$- (q is 0, 1 or 2); and/or (with the proviso that where R_{2s} is -SO_2- or -O-CO- not on the first carbon atom of the (1-6C) alkyl chain) optionally substituted by one or more groups (including geminal disubstitution) each independently selected from hydroxy and fluoro, and/or optionally monosubstituted by -NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl], (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino, N-(1-4C)alkyl-N-(1-6C)alkanoylamino, (1-4C)alkylS(O)$_p$NH- or (1-4C)alkylS(O)$_p$-((1-4C)alkyl)N- (p is 1 or 2)}; or

(ii) an optionally substituted aryl or heteroaryl group of the formula AR1, AR2, AR2a, AR2b, AR3, AR3a, AR3b, AR4, AR4a or CY all as defined (and optionally substituted as defined) herein.

10. A compound of the formula (I) as claimed in any one of claims 1 to 8, or a pharmaceutically acceptable salt, or in-vivo hydrolysable ester thereof, wherein:
when ms is 0, R_{2s} is selected from :

(i) hydrogen, (1-6C)alkyl {optionally monosubstituted by (1-4C)alkoxy, trifluoromethyl, (1-4C)alkylS(O)$_q$- (q is 0, 1 or 2); or optionally substituted by one or more fluoro-groups (including geminal disubstitution); or optionally substituted by one or more hydroxy groups (excluding geminal disubstitution)}; or

(iii) -CO-NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl], -CO-NRv Rw' [wherein Rv is hydrogen or (1-4C)alkyl; Rw' is phenyl (optionally substituted as for AR1 defined herein)], (1-4C)alkoxycarbonyl; and wherein
when ms is 1, E is -CO- or -SO_2- and R_{2s} is selected from :
(1-6C)alkyl {optionally monosubstituted by (1-4C)alkoxy, trifluoromethyl, (1-4C)alkylS(O)$_q$- (q is 0, 1 or 2); or optionally substituted by one or more fluoro groups (including geminal disubstitution); or optionally substituted by one or more hydroxy groups (excluding geminal disubstitution)}, (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino.

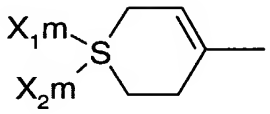
11. A compound of the formula (I) as claimed in any one of claims 1 to 10, or a pharmaceutically acceptable salt, or in-vivo hydrolysable ester thereof, wherein:

Rc is $R^{13}CO$- and R^{13} is selected from (1-4C)alkoxycarbonyl, hydroxy(1-4C)alkyl, (1-4C)alkyl (optionally substituted by one or two hydroxy groups, or by an (1-4C)alkanoyl group), (1-4C)alkylamino, dimethylamino(1-4C)alkyl, (1-4C)alkoxymethyl, (1-4C)alkanoylmethyl, (1-4C)alkanoyloxy(1-4C)alkyl, (1-5C)alkoxy and 2-cyanoethyl.

12. A compound of the formula (I) as claimed in any one of claims 1 to 11, or a pharmaceutically acceptable salt, or in-vivo hydrolysable ester thereof, wherein: R^{13} is 1,2-dihydroxyethyl, 1,3-dihydroxyprop-2-yl, 1,2,3-trihydroxyprop-1-yl, methoxycarbonyl, hydroxymethyl, methyl, methylamino, dimethylaminomethyl, methoxymethyl, acetoxymethyl, methoxy, methylthio, naphthyl, tert-butoxy or 2-cyanoethyl.

13. A compound as claimed in any preceding claim or pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof wherein HET(AR) is phenyl and at each occurrence R1 is independently hydrogen or fluorine.

14. A compound as claimed in any preceding claim, or pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof wherein T is TA1b:



(TA1b)

and wherein X_1m and X_2m are as defined in any one of the preceding claims.

15. A compound as claimed in any preceding claim, wherein said compound is selected from any one of:

cis and *trans*-(*5R*)-{3-[3-Fluoro-4-(1-imino-1-oxo-tetrahydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester;

(*5R*)-{3-[3-Fluoro-4-(*1RS*-1-imino-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester;

(*5S*)-3-[3-Fluoro-4-(*1RS*-1-imino-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-ylaminomethyl)-oxazolidin-2-one;

(*5S*)-*N*-(4-{2-Fluoro-4-[5-(isoxazol-3-yloxymethyl)-2-oxo-oxazolidin-3-yl]-phenyl}-*1RS*-1-oxo-,3,6-dihydrothiopyran-1-ylidene)-2-hydroxy-acetamide;

(*5R*)-{3-[3,5-Difluoro-4-(*1RS*-1-imino-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-2-oxo-oxazolidin-5-ylmethyl}-isoxazol-3-yl-carbamic acid *tert*-butyl ester;

(*5S*)-3-[3,5-Difluoro-4-(*1RS*-1-imino-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-ylaminomethyl)-oxazolidin-2-one;

(*5S*)-(4-{2,6-Difluoro-4-[5-(isoxazol-3-ylaminomethyl)-2-oxo-oxazolidin-3-yl]-phenyl}-*1RS*-1-oxo-3,6-dihydrothiopyran-1-ylidene)-carbamic acid methyl ester;

(*5S*)-1-(4-{2,6-Difluoro-4-[5-(isoxazol-3-ylaminomethyl)-2-oxo-oxazolidin-3-yl]-phenyl}-*1RS*-1-oxo-3,6-dihydrothiopyran-1-ylidene)-3-ethyl-urea;

(*5S*)-3-[3,5-Difluoro-4-(*1RS*-1-methylimino-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-ylaminomethyl)-oxazolidin-2-one;

(*5S*)-Ethanesulfonic acid (4-{2,6-difluoro-4-[5-(isoxazol-3-ylaminomethyl)-2-oxo-oxazolidin-3-yl]-phenyl}-*1RS*-1-oxo-3,6-dihydrothiopyran-1-ylidene)-amide;

Acetic acid (*5S*)-(4-{2,6-difluoro-4-[5-(isoxazol-3-ylaminomethyl)-2-oxo-oxazolidin-3-yl]-phenyl}-*1RS*-1-oxo-3,6-dihydrothiopyran-1-ylidenecarbamoyl)-methyl ester;

(*5S*)-*N*-(4-{2,6-Difluoro-4-[5-(isoxazol-3-yloxymethyl)-2-oxo-oxazolidin-3-yl]-phenyl}-*1RS*-1-oxo-3,6-dihydrothiopyran-1-ylidene)-2-hydroxy-acetamide;

(*5S*)-3-[3-Fluoro-4-(*1RS*-1-(acetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one;

(*5S*)-3-[3-Fluoro-4-(*1RS*-1-(*2S*-methyl-*2S*-acetoxyacetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one;

(*5S*)-3-[3-Fluoro-4-(*1RS*-1-(*2S*-methyl-*2S*-hydroxyacetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one;

(*5S*)-3-[3-Fluoro-4-(*1RS*-1-(2,2-dimethyl-2-acetoxyacetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one;

(*5S*)-3-[3-Fluoro-4-(*1RS*-1-(2,2-dimethyl-2-hydroxyacetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one;

(*5S*)-3-[3-Fluoro-4-(*1RS*-1-(*2R*-phenyl-*2R*-formyloxyacetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one;

(*5S*)-3-[3-Fluoro-4-(*1RS*-1-(*2R*-phenyl-*2R*-hydroxyacetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one;

(*5S*)-3-[3-Fluoro-4-(*1RS*-1-(2-isoxazol-5-yl-acetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one;
(*5S*)-3-[3-Fluoro-4-(*1RS*-1-(2-(3,5-dimethylisoxazol-4-yl)-acetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one;
(*5S*)-3-[3-Fluoro-4-(*1RS*-1-(2-(4-methyl-1,2,3-thiadiazol-5-yl)-acetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one; and
(*5S*)-3-[3-Fluoro-4-(*1RS*-1-(2-(1,3-dimethyl-pyrazol-5-yl)-acetylimino)-1-oxo-3,6-dihydrothiopyran-4-yl)-phenyl]-5-(isoxazol-3-yl-aminomethyl)-oxazolidin-2-one;
and pharmaceutically-acceptable salts and in-vivo hydrolysable esters thereof.

16. A compound of the formula (I) as claimed in any preceding claim, or a pharmaceutically-acceptable salt, or in-vivo hydrolysable ester thereof, for use as a medicament.

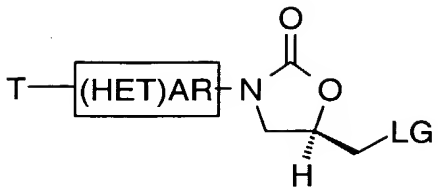
17. The use of a compound of the formula (I) as claimed in any preceding claim, or a pharmaceutically-acceptable salt, or in-vivo hydrolysable ester thereof, in the manufacture of a medicament for use in the production of an antibacterial effect in a warm blooded animal.

18. A pharmaceutical composition which comprises a compound of the formula (I) as claimed in any preceding claim, or a pharmaceutically-acceptable salt or an in-vivo hydrolysable ester thereof, and a pharmaceutically-acceptable diluent or carrier.

19. A method of manufacture of a compound as claimed in any preceding claim and pharmaceutically-acceptable salts and *in vivo* hydrolysable esters thereof, according to a process **(a)** to **(f)** as follows (wherein the variables are as defined above unless otherwise stated) :

(a) by modifying a substituent in or introducing a substituent into another compound of formula (I); or

(b) by reaction of a compound of formula (II) :



(II)

wherein LG is a displaceable group with a compound of the formula (III):

Y-Z

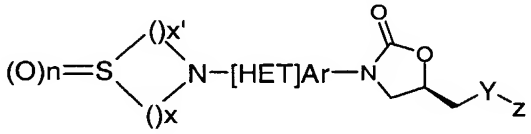
(III)

wherein heterocyclic compound Y-Z is appropriately derivatised for coupling with a compound of formula (II); or

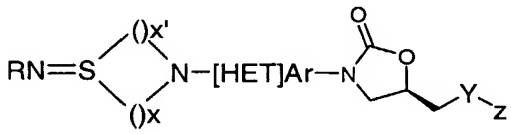
(c) by oxidation

(i) with an aminating agent of a lower valent sulfur compound (IV), or an analogue thereof, which is suitable to give a T substituent as defined by (TA2), or a bi-, or tri-cyclic ring analogue of (IV) which is suitable to give a T substituent as defined by (TB); or

(ii) with an oxygenating agent of a lower valent sulfur compound (V), or an analogue thereof, which is suitable to give a T substituent as defined by (TA2), or a bi-, or tri-cyclic ring analogue of (V) which is suitable to give a T substituent as defined by (TB);



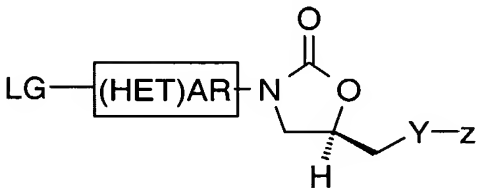
(IV)



(V)

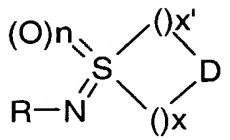
where n = 0 or 1 and ()x and ()x' are chains of length x and x'; or

(d)(i) by coupling of a compound of formula (VI) :



(VI)

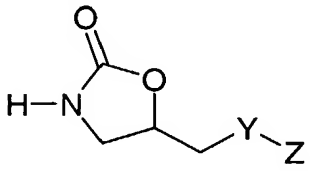
wherein Y-Z is as hereinbefore defined, LG is a replaceable substituent with a compound of the formula (VII), or an analogue thereof, which is suitable to give a T substituent as defined by (TA1), in which the link is via an sp^2 carbon atom, or (TA2), or a bi- or tri-cyclic ring analogue of (VII) which is suitable to give a T substituent as defined by (TB);



(VII)

where n = 0 or 1 and ()x and ()x' are chains of length x and x'; D is NH or CH=C-Lg where Lg is a leaving group; or

(d) (ii) by coupling, of a compound of formula (VIII):



(VIII)

wherein Y-Z is as hereinbefore defined, with a compound [Aryl]-LG, where LG is a replaceable substituent; or

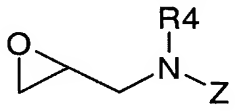
(e) by reduction of a compound formed by process (d) in which the T substituent (as defined by (TA1)) is linked via an sp^2 carbon atom, to form the saturated analogue; or

(f) by reaction of a compound of the formula (IX) :

T-Q-Z(f)

(IX)

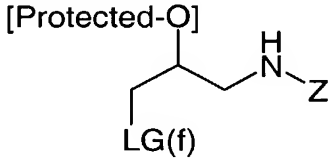
wherein Z(f) is an isocyanate, amine or urethane group with an epoxide of the formula (X):



(X)

wherein Z is an heteroaromatic group as hereinabove defined;

or with a related compound of formula (XI) where the hydroxy group at the internal C-atom is optionally conventionally protected and where the leaving group LG(f) at the terminal C-atom is a conventional leaving group.



(XI)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 02/01626

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D413/14 C07D417/14

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 99 64417 A (ZENECA LTD ;GRAVESTOCK MICHAEL BARRY (GB)) 16 December 1999 (1999-12-16) cited in the application page 12, line 24 -page 13, line 14; claims 1,4 ---	1-19
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the International search	Date of mailing of the International search report
5 June 2002	17/06/2002

Name and mailing address of the ISA	Authorized officer
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International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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Y	WO 95 07271 A (UPJOHN CO ;BARBACHYN MICHAEL R (US); BRICKNER STEVEN J (US); HUTCH) 16 March 1995 (1995-03-16) Chart 2, compounds 14 page 2, line 1 -page 2, line 28; claim 1	1-19
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P,Y	WO 01 46185 A (ALEXANDER DAVID L ;HESTER JACKSON B JR (US); UPJOHN CO (US)) 28 June 2001 (2001-06-28) claim 1, examples	1-19
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A	WO 96 15130 A (UPJOHN CO ;BARBACHYN MICHAEL R (US); THOMAS RICHARD C (US); CLEEK) 23 May 1996 (1996-05-23) claim 1	1

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